Novel Polycyclic Heterocycles. VIII. 6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocines and their Derivatives (1,2)

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Received March 2, 1972

6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine, **4**, and its 2-chloro, **7**, and 2-(trifluoromethyl)-, **1**, derivatives, were prepared by the reaction of an *o*-aminobenzenethiol and α,α-dibromo-*o*-xylene. Acylation and alkylation at position-12 gave a series of ω-haloacyl-, ω-aminoacyl, and ω-aminoalkyl derivatives of these heterocycles. The conformations, proton magnetic resonance spectra, and x-ray crystallographic studies of these compounds are discussed.

In earlier papers, we have reported the synthesis of the isomeric 10,11-dihydrodibenzo[*b*,*f*][1,4]thiazepines (4) and 5,11-dihydrodibenzo[*b*,*e*][1,4]thiazepines (5), the 5,11-dihydrodibenz[*b*,*e*][1,4]oxazepines (5,6), and their derivatives. In this paper, we describe the preparation of homologous *thia* heterocycles, the 6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocines and their derivatives, while in the following paper (7), we are reporting the synthesis of the *oxa* analogs, the 6,11-dihydro-12*H*-dibenz[*b*,*f*][1,4]-oxazocines and their derivatives.

The *thiazocines* were prepared by the reaction of an *o*-aminobenzenethiol or its zinc salt and α, α′-dibromo-*o*-xylene in dimethylformamide (8). The products were readily isolated from the reaction mixtures as their highly

CHART I

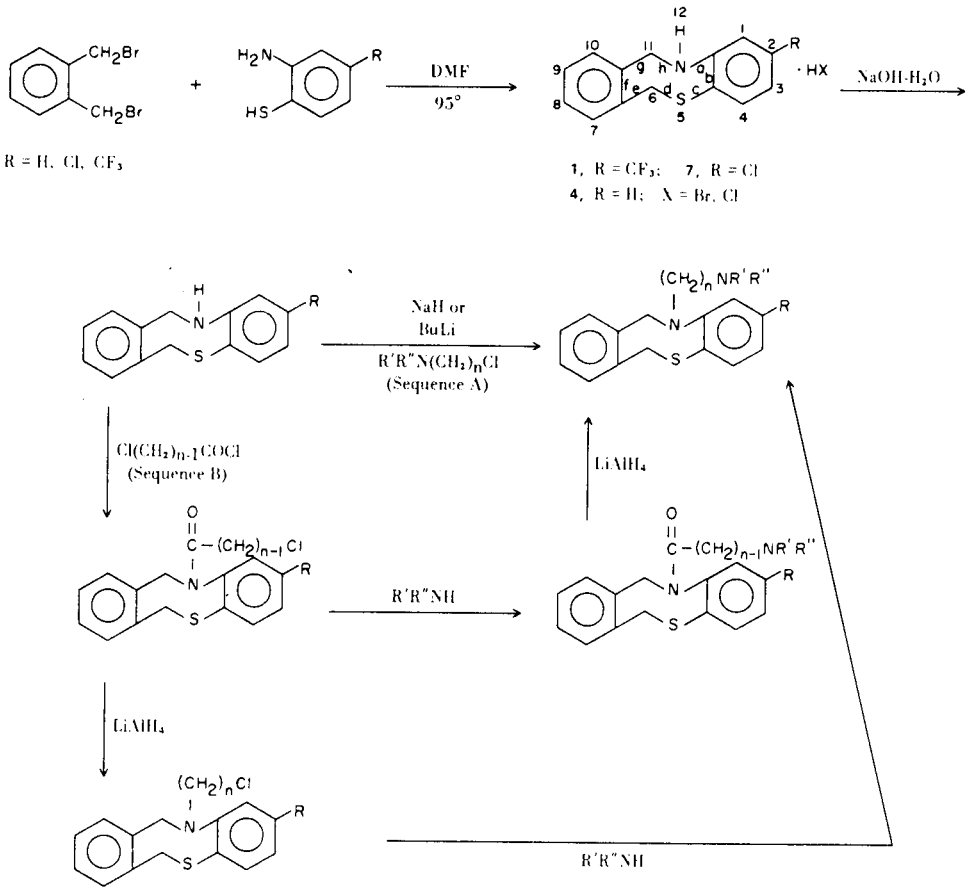


TABLE Ia

Derivatives of 6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocines

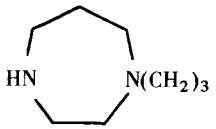
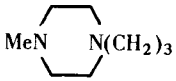
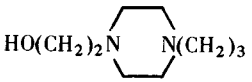
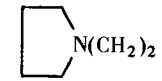
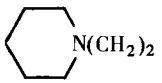
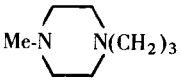
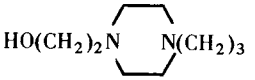
No.	Method (b)	X	R	Yield (a) %	Formula	BASES B.p. (mm) or M.p., °C	Recrystn. Solvent	Analyses Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	F	H	$Me_2N(CH_2)_2$	85	$C_{18}H_{22}N_2S$	(c)				9.38 (d)			9.40
2	G	H	$Et_2N(CH_2)_2$	57	$C_{20}H_{26}N_2S$	171-173 (0.5)		73.57	8.03	8.58	73.60	7.77	8.34
3	F	H	$MeNH(CH_2)_3$	79	$C_{18}H_{22}N_2S$	146-148 (0.15)		72.44	7.43	9.38	72.29	7.59	9.64
4	E,F	H	$Me_2N(CH_2)_3$	58, 70	$C_{19}H_{24}N_2S$	(c)							
5	H	Cl	$Me_2N(CH_2)_2$	20	$C_{18}H_{21}ClN_2S$	74-75	E			8.42 (n)			8.36
6	E,F	CF_3	$Me_2N(CH_2)_3$	64, 78	$C_{20}H_{23}F_3N_2S$	48-50	F	63.15	6.09	7.36	63.40	6.09	7.32
7	F	CF_3	$Et_2N(CH_2)_3$	90	$C_{22}H_{27}F_3N_2S$	(c)				6.85 (k)			7.13
8	H	CF_3	$Me_2NCHMeCH_2$	85	$C_{20}H_{23}F_3N_2S$	155-160 (0.3) 69-70	E	63.15	6.09	7.36	63.28	6.16	7.30
9	F	H		77	$C_{22}H_{29}N_3S$	(c)		71.88	7.95	11.43	71.82	7.99	11.57
10	F	H		89	$C_{22}H_{29}N_3S$	(c)		71.88	7.95	11.43	71.59	8.05	11.70
11	F	H		77	$C_{23}H_{31}N_3OS$	(c)		69.47	7.86	10.57	69.24	8.14	10.13
12	H	Cl		84	$C_{20}H_{23}ClN_2S$	190-193 (0.05)		66.91	6.46	7.80 (q)	66.70	6.34	7.66
13	H	Cl		79	$C_{21}H_{25}ClN_2S$	107-109	K	67.62	6.76	7.51	67.77	6.77	7.30
14	F	CF_3		77	$C_{23}H_{28}F_3N_3S$	84-86	F			9.64 (t)			9.45
15	F	CF_3		81	$C_{24}H_{30}F_3N_3OS$	(c)				9.02 (v)			8.89

TABLE Ia (continued)

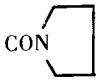
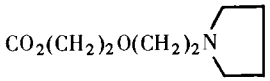
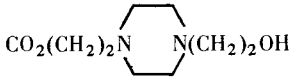
No.	Method (b)	X	R	Yield (a) %	Formula	B.p. (mm) or M.p., °C	Recrystn. Solvent	BASES Analyses Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
16	D	H	$COCH_2NMe_2$	67	$C_{18}H_{20}N_2OS$	141-143	L			8.96 (x)			9.05
17	I	H	$CO(CH_2)_2NMe_2$	89	$C_{19}H_{22}N_2OS$	134-136	M	69.89	6.79	8.58	70.05	6.64	8.46
18	D	Cl	$COCH_2NMe_2$	77	$C_{18}H_{19}ClN_2OS$	121-123	F			9.23 (y)			9.18
19	D	CF_3	$CO(CH_2)_2NMe_2$	90	$C_{20}H_{21}F_3N_2OS$	112-113	N			7.12 (z)			7.18
20	D	CF_3	$CO(CH_2)_2NEt_2$	95	$C_{22}H_{25}F_3N_2OS$	53-55	F			6.63 (aa)			6.56
21	D	CF_3	$CO(CH_2)_2N(CH_2)_4NMe$	85	$C_{23}H_{26}F_3N_3OS$	150-152	L			9.34 (cc)			9.36
22	D	CF_3	$CO(CH_2)_2N(CH_2)_4N(CH_2)_2OH$	60	$C_{24}H_{28}F_3N_3O_2S$	137-139	L	60.10	5.88	8.76 (dd)	60.12	6.05	8.91
23	K	H	$CONH_2$	56	$C_{15}H_{14}N_2OS$	213-215	I			10.36 (ee)			10.26
24	K	Cl	$CONH_2$	54	$C_{15}H_{13}ClN_2OS$	223-225 dec.	I			9.91 (ff)			9.70
25	K	CF_3	$CONH_2$	61	$C_{16}H_{13}F_3N_2OS$	253-255	I			8.28 (gg)			8.24
26	O	H	$CSNH_2$	33	$C_{15}H_{14}N_2S_2$	239-241 dec.	O	62.90	4.92	9.78	62.86	4.63	9.92
27	P	H	$CONEt_2$	47	$C_{19}H_{22}N_2OS$	126-128	P	69.89	6.79	8.58	69.78	6.98	8.53
28	L	H	$CONHCH_2CH_2NMe_2$	68	$C_{19}H_{23}N_3OS$	138-139	M	66.82	6.79	12.30	66.48	6.41	12.12
29	L	H	$CONH(CH_2)_3NMe_2$	49	$C_{20}H_{25}N_3OS$	121-122	M	67.56	7.09	11.82	67.53	6.90	11.46
30	M	H	$CONHCH_2CH_2NEt_2$	C									
31	M	H	$CONH(CH_2)_3NEt_2$	C									
32	L	H		76	$C_{20}H_{19}F_3N_2OS$	185-187	I	61.22	4.87	7.13	61.24	4.96	7.08
33	N	H	$CO_2CH_2CH_2NMe_2$	C									
34	N	H	$CO_2(CH_2)_4NMe_2$	C									
35	N	H		30	$C_{24}H_{30}N_2O_3S$	69-71	F	67.56	7.09	6.56	67.57	6.81	6.48
36	N	H		69	$C_{23}H_{29}N_3O_3S \cdot 0.5H_2O$	97-99	M	63.27	6.93		63.56	6.82	

TABLE Ib

Salts of Derivatives of 6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocines

No.	Yield (a) %	Formula	M.p., °C	Recrystn. Solvent	SALTS Analyses Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1	54	$C_{18}H_{22}N_2S \cdot C_4H_4O_4$	134-135	A			6.73 (e)			6.58
2	59	$C_{20}H_{26}N_2S \cdot HCl$	179-180	B			7.72 (f)			7.59
3	72	$C_{18}H_{22}N_2S \cdot C_4H_4O_4$	145-146	C	63.74	6.32	6.76	63.44	6.35	6.51
4	47	$C_{19}H_{24}N_2S \cdot C_2H_2O_4$	171-172	D	62.66	6.51	6.96 (g)	62.80	6.25	7.06
5	73	$C_{18}H_{21}ClN_2S \cdot C_4H_4O_4$	123-125	A			(i)			
6	78	$C_{20}H_{23}F_3N_2S \cdot C_2H_2O_4$	193-195	D	56.15	5.35	5.95 (j)	56.39	5.52	6.03
	73	$C_{20}H_{23}F_3N_2S \cdot HCl \cdot H_2O$	148-150	G	55.19	6.02	(l)	55.17	6.13	
7	75	$C_{22}H_{27}F_3N_2S \cdot HCl$	146-148 dec.	G	59.37	6.34	6.29 (m)	59.15	6.42	5.97
8	61	$C_{20}H_{23}F_3N_2S \cdot HCl \cdot 0.5H_2O$	183-185	H	56.38	5.92	6.58 (n)	56.77	5.88	6.41
9	22	$C_{22}H_{29}N_3S \cdot 2C_4H_4O_4$	150-152 dec.	I	60.08	6.22	7.00	60.18	6.36	7.27
10	70	$C_{22}H_{29}N_3S \cdot 3HCl \cdot 0.25H_2O$	220-222 dec.	J	54.88	6.80	8.73 (o)	54.84	7.02	8.61
11	65	$C_{23}H_{31}N_3OS \cdot 3HCl$	203-205	D	54.49	6.77	8.29 (p)	54.34	7.05	8.07
12	80	$C_{20}H_{23}ClN_2S \cdot HCl$	209-211 dec.	A	60.74	6.12	7.08 (r)	60.65	6.25	6.93
13	44	$C_{21}H_{25}ClN_2S \cdot HCl$	215-217 dec.	A	61.59	6.40	6.84 (s)	61.83	6.35	6.73
14	62	$C_{23}H_{28}F_3N_3S \cdot 2HCl$	232-234 dec.	I			8.26 (u)			8.38
15	79	$C_{24}H_{30}F_3N_3OS \cdot 2HCl$	225-227 dec.	D			7.80 (w)			7.70
16										
17										
18										
19										
20	81	$C_{22}H_{25}F_3N_2OS \cdot HCl$ (b)	171-173 dec.	H			6.10 (bb)			6.15
21										
22										
23										
24										
25										
26										
27										
28										
29										
30	10	$C_{21}H_{27}N_3OS \cdot HCl$	202-204 dec.	H	(hh)					
31	33	$C_{22}H_{29}N_3OS \cdot HCl$	193-194 dec.	A	(ii)					
32										
33	40	$C_{19}H_{22}N_2O_2S \cdot HCl$	168-169	Q	60.23	6.12 (jj)		60.10	5.85	
34	52	$C_{21}H_{26}N_2O_2S \cdot C_2H_2O_4 \cdot H_2O$	116-117	D	57.72	6.31	5.85	57.37	6.38	5.92
35										
36	42	$C_{23}H_{29}N_3O_3S \cdot 2C_2H_2O_4$	185-187 dec.	R	53.37	5.47	6.92	53.63	5.45	6.53

Recrystallization Solvents: A = 2-propanol; B = acetonitrile-ethyl ether; C = MEK; D = absolute ethanol; E = 95% ethanol; F = Ligroin; G = 1.5% aqueous hydrochloric acid; H = ethyl acetate; I = acetonitrile; J = absolute ethanol-ethyl ether; K = Hexane; L = Cyclohexane; M = Skellysolve E; N = petroleum ether; O = Benzene; P = Diisopropyl ether; Q = Chlorobenzene; R = 1-propanol.

Footnotes - Tables Ia and Ib: (a) The yield given involves the last reaction of any synthetic sequence. (b) See Experimental Section. (c) Not distilled; crude base was converted to its salt. (d) *Anal.* Calcd.: S, 10.74; N.E. (perchloric acid), 150. Found: S, 10.70; N.E., 154. (e) *Anal.* Calcd.: S, 7.73; N.E. (perchloric acid), 207. Found: S, 7.70; N.E., 210. (f) *Anal.* Calcd.: Cl, 9.77. Found: Cl, 9.92. (g) *Anal.* Calcd.: S, 7.97. Found: S, 7.60. (h) *Anal.* Calcd.: Cl, 10.64; S, 9.62. Found: Cl, 10.68; S, 9.78. (i) *Anal.* Calcd.: Cl, 7.89; S, 7.12; N.E. (sodium hydroxide), 225. Found: Cl, 7.90; S, 7.15; N.E., 223. (j) *Anal.* Calcd.: N.E. (sodium hydroxide), 236. Found: N.E., 233. (k) *Anal.* Calcd.: S, 7.84. Found: S, 7.99. (l) *Anal.* Calcd.: Cl, 8.15. Found: Cl, 8.08. (m) *Anal.* Calcd.: Cl, 7.96. Found: Cl, 8.08. (n) *Anal.* Calcd.: Cl, 8.32. Found: Cl, 8.51. (o) *Anal.* Calcd.: Cl, 22.09. Found: Cl, 22.35. (p) *Anal.* Calcd.: Cl, 20.98. Found: Cl, 20.94. (q) *Anal.* Calcd.: N.E. (perchloric acid), 359. Found: 355. (r) *Anal.* Calcd.: Cl, 17.93. Found: Cl, 17.55. (s) *Anal.* Calcd.: Cl, 17.32. Found: Cl, 17.44. (t) *Anal.* Calcd.: S, 7.36. Found: S, 7.15. (u) *Anal.* Calcd.: Cl, 13.92; S, 6.34. Found: Cl, 14.12; S, 6.39. (v) *Anal.* Calcd.: S, 6.88. Found: S, 7.00. (w) *Anal.* Calcd.: Cl, 13.16; S, 5.95. Found: Cl, 13.00; S, 6.00. (x) *Anal.* Calcd.: S, 10.26; N.E. (perchloric acid), 312. Found: S, 10.19; N.E. 309. (y) *Anal.* Calcd.: Cl, 10.21; S, 9.23. Found: Cl, 10.15; S, 9.18. (z) *Anal.* Calcd.: S, 8.12. Found: S, 8.38. (aa) *Anal.* Calcd.: S, 7.58. Found: S, 7.75. (bb) *Anal.* Calcd.: Cl, 7.74. Found: Cl, 7.62. (cc) *Anal.* Calcd.: S, 7.13. Found: S, 7.43. (dd) *Anal.* Calcd.: S, 6.68. Found: S, 6.96. (ee) *Anal.* Calcd.: S, 11.93. Found: S, 12.08. (ff) *Anal.* Calcd.: Cl, 11.63; S, 10.51. Found: Cl, 11.54; S, 10.43. (gg) *Anal.* Calcd.: S, 9.47. Found: S, 9.64. (hh) *Anal.* Calcd.: Cl, 8.73; N.E. (perchloric acid), 400. Found: Cl, 8.65; N.E., 406. (ii) *Anal.* Calcd.: Cl, 8.44; S, 7.63. Found: Cl, 8.70; S, 7.47. (jj) *Anal.* Calcd.: Cl, 9.36. Found: Cl, 9.40.

insoluble hydrohalide salts. The crystalline, ether-soluble thiazocines were recovered when these salts were shaken with aqueous alkali and ether.

While the anions of these heterocycles could be generated with sodium hydride or with *n*-butyllithium in hydrocarbon solvents and alkylated with several dialkylaminoethyl chlorides or bromides (Sequence A), the more generally applicable procedure involved the initial preparation of the 12-ω-chloroacyl derivative and conversion of the latter, by two routes (Sequence B) into the aminoalkyl derivatives. These reactions are summarized in Chart I.

As noted above, the heterocycles formed monohydrobromides and -hydrochlorides. The simple dialkylaminoalkyl and dialkylaminoacyl derivatives behaved as monoacidic bases and formed 1:1 hydrochloride, maleate, and oxalate salts. The homopiperazine derivative also behaved normally, forming a dimaleate; unexpectedly, and there is no explanation for this, the piperazine derivatives formed trihydrochlorides.

In contrast to the failure of the 5,11-dihydrodibenz[*b*,*e*][1,4]oxazepines and 5,11-dihydrodibenzo[*b*,*e*][1,4]thiazepines to undergo *N*-formylation (5), the thiazocines reacted readily with 98-100% formic acid to give *N*-formyl derivatives in excellent yields, and with acetic anhydride to give *N*-acetyl derivatives.

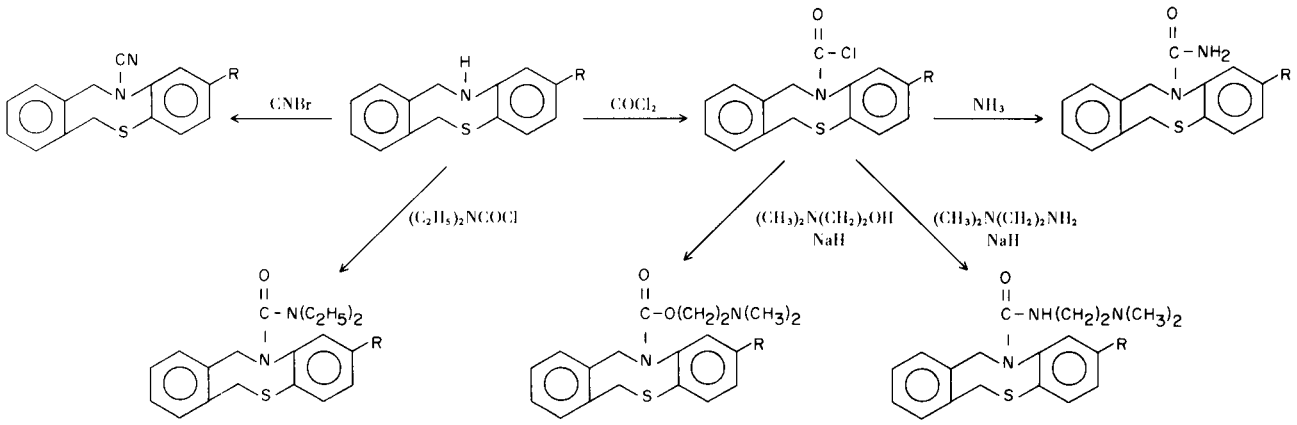
The thiazocines also reacted with phosgene to form crystalline carbamoyl chlorides, and this behavior, again, was in contrast to that observed with the 5,11-dihydrodibenzo[*b*,*e*][1,4]thiazepines and -oxazepines, where the corresponding derivatives have never been isolated and characterized (9). The carbamoyl chlorides, (a) with ethanolic ammonia gave ureas, (b) with dialkylaminoalkanols yielded urethanes, and (c) with dialkylaminoalkylamines gave carbamates. *N*,*N*-Dialkylcarbamoyl chlorides and the thiazocines gave the *N*,*N*-dialkylureas while cyanogen bromide gave the cyanamide derivative. These reactions are summarized in Chart II.

The physical properties and analytical data for the derivatives of the 6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]-thiazocines are found in Table I.

Conformations of 6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]-thiazocines.

Dreiding models of the thiazocine heterocycle suggest that two possible conformations are possible. One is a somewhat rigid form, incapable of ready interconversion into another conformation; the other is a non-rigid form that readily interconverts to a second, non-rigid counterpart. Figure I, *a* and *b*, respectively, show line drawings made from photographs of the Dreiding models of the non-rigid and rigid forms; it is the latter conformation that is seen in the single crystal structure, as determined by X-ray analysis (see below).

CHART II



Single Crystal Structure Analysis of I-24 (10).

Crystals of I-24 [2-chloro-6,11-dihydro-6*H*-dibenzo-[*b*,*f*][1,4]thiazocine-12-carboxamide] grown from acetonitrile solutions were found to be monoclinic with a = 14.45, b = 14.08, c = 14.41Å and β = 104.8°. Systematically absent X-ray reflections and the crystal density measured by flotation methods (1.432g/cm^3) suggested space group $P2_1/c$ with two molecules in the asymmetric unit. The analysis accordingly required the determination of forty atomic positions excluding hydrogen atoms. Diffraction intensities from reciprocal lattice layers h0ℓ through h6ℓ and hk0 through hk2, were recorded photographically by the equi-inclination Weissenberg method (CuKα) and estimated through visual comparisons with a reference intensity scale. The data were converted to $|F|^2$ and correlated to produce the final set of 1,434 reflections used in the analysis. The coordinates of the four crystallographically independent heavy atoms were obtained from a sharpened Patterson map and used to compute approximate phase angles for an electron density synthesis. All thirty-six of the remaining non-hydrogen atoms were located in this initial Fourier map.

As anticipated, the asymmetric unit contains two distinct though chemically identical molecules which appear to be joined through mutual hydrogen bonds from the primary amide group of each molecule to the carbonyl oxygen atom of the other. At the present, initial, stages of refinement (R = .20), these molecules appear to have qualitatively equivalent conformations which will be described with reference to the atoms, 1 through 20, of one molecule. The "basket-like" conformation of the tricyclic nucleus can be described by three planes approximately containing: (A) atoms 1 through 8, and 17, (B) atoms 9 through 16, and (C) atoms 8, 9, 16, 17. The dihedral angles defined by A and C, B and C, and A and B are 140, 113, and 74° respectively. The torsional angles

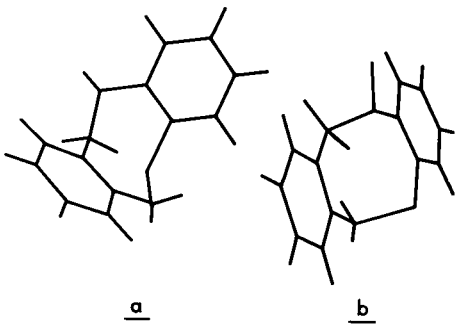


Fig. 1. Non-rigid (a) and rigid (b) conformations of the 6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine heterocycle.

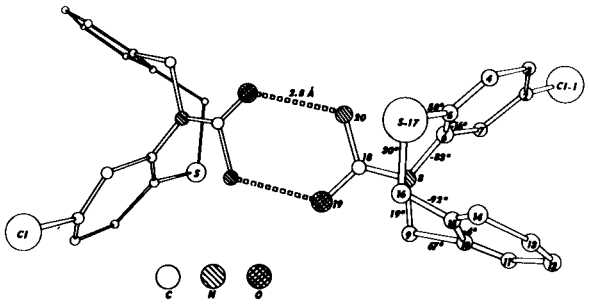


Fig. 2. The pseudocentric hydrogen-bonded arrangement of the two independent molecules in the asymmetric unit of the crystal structure of I-24.

around the eight membered ring are shown in Figure 2. The orientation of the urea group relative to the cyclic nucleus defines the torsional angles O(19) - C(18) - N(8) - C(6) = 180° and C(18) - N(8) - C(6) - C(7) = -92°.

The molecular structure accordingly is chiral and the crystal structure is a racemate comprised of both enantiomers related through crystallographically required improper symmetry elements. Interestingly, the two independent molecules of the asymmetric unit also are *enantiomers* which are related through an approximate noncrystallographic inversion center at (0.25, 0.96, 0.10) relative to the space group inversion center at the origin of axes. The mutual hydrogen bonding of these two molecules across the pseudocenter (Figure 2) is reminiscent of the centrosymmetric "dimeric" hydrogen bonding mode commonly found in crystal structures of carboxylic acids.

Proton Magnetic Resonance Spectra.

The pmr spectrum of 12-benzyl-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**20**) showed two singlets at δ 4.68 and 4.36, that integrated in a ratio of 2H:4H, respectively. Thus, the signal at δ 4.68 can be assigned to the CH_2 group at position-6 and the signal at δ 4.36 can be attributed to the two equivalent CH_2 groups attached to the heterocyclic nitrogen atom. The pmr spectrum of 6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**4**) showed two 2-proton singlets at δ 4.74 and 4.29, attributed to the methylene protons at positions -6 and -11, respectively. With substitution at position -2 by chlorine (**7**) or trifluoromethyl (**1**) the signals were still seen as singlets, and no significant chemical shift had occurred, *i.e.*, the signals were seen at δ 4.78 and 4.31 and at δ 4.78 and 4.31 respectively. When the proton at position -12 was replaced by -C(=O)-Cl, as in **17**, the two methylene groups at positions -6 and -11 were seen as A_2B_2 systems, with the quartets centered at δ 4.46 and 3.78 (J = 15) and at δ 5.80 and 4.34 (J = 13). When the same proton was replaced by -C(=S)-Cl, as in **19**, the effects were even more marked; the signals were at δ 4.80 and 3.80 (J = 15) and at δ 6.67 and 4.50 (J = 13).

These anisotropic effects of carbonyl oxygen or thiocarbonyl sulfur (11) in shielding and deshielding the methylene protons at positions -6 and -11 and consequently inducing striking chemical shifts and splitting of the signals as described above for **17** and **19** were also seen when the 12-substituent was -C(=O)-CH_3, -C(=O)-$(CH_2)_n$Cl, -C(=O)-$(CH_2)_n$$NR_2$, -C(=O)-$NH_2$, C(=O)-NH- and C(=O)-O; when the 12-substituent was -C(=O)-H, -C(=O)-$N(C_2H_5)_2$, or -C(=O)-N⟨ ⟩, the signals were seen as broad singlets; and, finally, when the 12-substituent was -$(CH_2)_n$Cl or -$(CH_2)_n$$NR_2$, the signals were restored to that seen when the 12-substituent was hydrogen or benzyl.

It was of interest, also that in 6,11-dihydrodibenzo[*b*,*f*][1,4]thiazocin-11(12*H*)one (8), the methylene protons at position-6 were equally affected by carbonyl oxygen, and were seen as an A_2B_2 quartet, with the two doublets centered at δ 4.57 and 4.00 (J = 13).

EXPERIMENTAL

The ir spectra were determined on mineral oil mulls or on solutions in deuteriochloroform by means of a Perkin Elmer spectrophotometer and the pmr spectra were carried out with a Varian A-60. The authors are indebted to Mrs. Barbara Toeplitz, and Drs. A. Cohen and M. Puar for these spectra. The microanalyses were carried out by Mr. J. Alicino and his associates. The melting points were determined in an electrically heated oil bath and are not corrected.

In the text below, compounds listed in Table I are identified by an Arabic number that carries the prefix, I-; all other compounds are identified by simple Arabic numbers.

6,11-Dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**1**). Method A.

To 10.5 g. (0.04 mole) of α, α′-dibromo-*o*-xylene in 200 ml. of anhydrous DMF at 95°, under nitrogen, and with stirring, was added in 0.5 hour, 18.0 g. (0.04 mole) of the zinc salt of 2-amino-α,α,α-trifluoro-*p*-toluenethiol (12) in 200 ml. of anhydrous DMF. Subsequently, the mixture was stirred at 95° for 0.5 hour and concentrated *in vacuo*. The residue was extracted with 400 ml. of ether, the extracts filtered, the filtrate washed with water, dried, and treated with ethereal hydrogen chloride to give 10.0 g. of crude *hydrochloride* (**2**), m.p. 192-200°. An analytical sample prepared by sublimation had a m.p. of 210-212°, ν (mull) 2450 (m), 1620 (w), 1550 (s), 1450 (s) cm^{-1}.

Anal. Calcd. for $C_{15}H_{12}F_3NS$·HCl: C, 54.29; H, 3.94; N, 4.22; Cl, 10.65. Found: C, 54.27; H, 3.96; N, 4.46; Cl, 10.68.

A suspension of 9.0 g. (0.027 mole) of crude **2** in 27 ml. of 10% aqueous potassium hydroxide and 100 ml. of ether was agitated until two clear phases formed, the ether layer was separated, dried, concentrated, and the residue recrystallized from pentane to give 4.0 g. (50% yield) of **1**, m.p. 87-89°; ν (mull) 3350 (m), 1600 (m), 1465 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.40-6.80 (m, 7*ar* H), 4.78 (s, 2H, position-6), 4.31 (s, 2H, position-11), 3.89 (broad s, 1H, *NH*).

Anal. Calcd. for $C_{15}H_{12}F_3NS$: C, 61.00; H, 4.08; N, 4.74; S, 10.85. Found: C, 60.80; H, 4.31; N, 5.03; S, 11.02.

6,11-Dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine-12-carboxaldehyde (**3**).

A solution of 5.0 g. (0.017 mole) of **1** and 50 ml. of 98-100% formic acid was heated under reflux for three hours, cooled to room temperature, and poured into 300 ml. of ice-water. The gum that separated was extracted into ether, the ether solution was washed, dried, and concentrated to give 4.8 g. of crude product, m.p. 125-127°. Recrystallization from hexane gave 4.0 g. (74% yield) of **3**, m.p. 125-126°; ν (mull) (no NH, 1680 (s), 1610 (m), 1480 (m), 1460 (m), 1430 (m) cm^{-1}; pmr (deuteriochloroform) δ 8.17 (s, 1H, CHO), 7.5-7.0 (m, 7 ar H), 5.1 (broad s, 2H, position-11), 4.12 (s, 2H, position-6).

Anal. Calcd. for $C_{16}H_{12}F_3NOS$: C, 59.44; H, 3.74; N, 4.34. Found: C, 59.40; H, 3.77; N, 4.28.

6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine, **4**. Method B.

To 13.2 g. (0.05 mole) of α,α′-dibromo-*o*-xylene in 250 ml. of anhydrous DMF at 90-95°, under nitrogen, was added in 0.33 hour a solution of 6.2 g. (0.05 mole) of *o*-aminobenzenethiol in 150 ml. of anhydrous DMF. Subsequently, the mixture was heated 0.5 hour at 90-95° and worked up as above to give 10.5 g. (70% yield) of **4**·*HBr* (**5**), m.p. 228-230°; ν (mull) 3350 (w), 2770-2410 (multiplet, m), 1560 (m), 1450 (s), 1375 (s) cm^{-1} The **5** was too insoluble to recrystallize and was instead leached repeatedly with acetonitrile and dried *in vacuo* at 80°.

Anal. Calcd. for $C_{14}H_{13}NS$·HBr: Br, 25.93; N, 4.54. Found: Br, 25.60; N, 4.59.

To 10.0 g. of 85% potassium hydroxide in 250 ml. of water, at 100°, was added 20.0 g. (0.065 mole) of **5**, the whole stirred at 100° until no solid remained, cooled to 25°, and extracted with ether. The ether solution was worked up to give 10.5 g. (70% yield) of **4**, m.p. 102-104° after recrystallization from cyclohexane; ν (mull) 3320 (w), 1590 (m), 1466 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.4-6.5 (m, 8 ar H), 4.74 (s, 2H, position-6), 4.29 (s, 2H, position-11), 3.67 (broad s, H of N*H*).

Anal. Calcd. for $C_{14}H_{13}NS$: C, 6.16; S, 14.10. Found: N, 6.31; S, 14.23.

6,11-Dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine-12-carboxaldehyde (**6**).

The above procedure with **4** and 98-100% formic acid gave **6** in 70% yield, m.p. 143-145° dec. after recrystallization from hexane; ν (mull) no NH, 1665 (s), 1560 (m), 1468 (s) cm^{-1}: pmr (deuteriochloroform) δ 8.29 (s, 1H, C*H*O), 7.3-6.9 (m, 8 ar H), 5.05 (broad s, 2H, position-11), 3.91 (s 2H, position-6).

Anal. Calcd. for $C_{15}H_{13}NOS$: C, 70.57; H, 5.14; N, 5.49. Found: C, 70.86; H, 5.08; N, 5.53.

12-Acetyl-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**7**).

A solution of 2.0 g. (0.009 mole) of **4**, 0.1 g. *p*-toluenesulfonic acid, and 20 ml. of acetic anhydride was heated at 110° for 1.5 hours, cooled, and poured into 200 ml. of ice-water. The solid that separated was filtered and dried to give 2.0 g. of crude **7**, m.p. 124-126°. Recrystallization from hexane gave 1.3 g. of **7**, m.p. unchanged; ν (mull) 1655 (s), 1470 (s), 1440 (s), 1390 (s), 1360 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.0-6.5 (m, 8 ar H), 6.0, 3.75 (A_2B_{2q}, J = 16, 2H, position-11), 4.20, 3.37 (A_2B_{2q}, J = 12, 2H, position-6), 1.56 (s, 3H of CH_3).

Anal. Calcd. for $C_{16}H_{15}NOS$: C, 71.37; H, 5.61; N, 5.20; S, 11.99. Found: C, 71.14; H, 5.78; N, 5.02; S, 11.45.

2-Chloro-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**8**).

Method B was employed to prepare **8**·HBr, (**9**) in 55% yield, m.p. 210-212° dec. after recrystallization from 95% ethanol; ν (mull) 3500 (w), 1570 (m), 1450 (s) cm^{-1}.

Anal. Calcd. for $C_{14}H_{12}ClNS$·HBr: C, 49.06; H, 3.82; Br, 23.32; N, 4.08. Found: C, 49.19; H, 3.92; Br, 23.54; N, 4.19.

From **9**, as above, there was recovered **8** in 78% yield, m.p. 138-140° after recrystallization from cyclohexane; ν (mull) 3390 (s), 1580 (s), 1490 (s), 1465 (s), 1450 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.33-6.5 (m, 7 ar H), 4.78 (s, 2H, position-6),4.31 (s, 2H, position-11), 3.85 (broad s, H of N*H*).

Anal. Calcd. for $C_{14}H_{12}ClNS$: C, 64.22; H, 4.62; Cl, 13.54; S, 12.24. Found: C, 64.50; H, 4.92; Cl, 13.75; S, 12.16.

2-Chloro-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine-12-carboxaldehyde (**10**).

The reaction of **8** with 90-100% formic acid as described above gave **10** in 60% yield, m.p. 173-175° dec., after recrystallization from acetonitrile; ν (mull) 1665 (s), 1630 (m), 1570 (m), 1490 (m), 1460 (s) cm^{-1}; pmr (deuteriochloroform) δ 8.16 (s, H of C*H*O), 7.33-7.0 (m, 7 ar H), 5.03 (broad s, 2H, position-11), 4.10 (s, 2H, position-6).

Anal. Calcd. for $C_{15}H_{12}ClNOS$: C, 62.17; H, 4.18; N, 4.84. Found: C, 62.33; H, 4.13; N, 4.76.

12-(3-Chloropropionyl)-6,11-dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine, (**11**). Method C.

A solution of 5.9 g. (0.02 mole) of **1** and 5.1 g. (0.04 mole) of 3-chloropropionyl chloride in 100 ml. of anhydrous toluene was heated for 2 hours under reflux, concentrated *in vacuo*, and the residue recrystallized from hexane to give 5.4 g. (76% yield) of **11**, m.p. 128-129°; ν (mull) 2860 (s), 1650 (s), 1475 (m), 1455 (m), 1420 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.50-6.80 (m, 7 ar H) 6.24, 4.13 (A_2B_{2q}, J = 15, 2H, position-11), 4.53, 3.76 (A_2B_{2q}, J = 15, 2H, position-6), 3.53 (m, 4H, -C(=O)CH_2CH_2Cl.

Anal. Calcd. for $C_{18}H_{15}F_3ClNOS$: Cl, 9.19; N, 3.63; S, 8.31. Found: Cl, 9.21; N, 3.92; S, 8.48.

12-[3-(Dimethylamino)propionyl]-6,11-dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (I-19). Method D.

A solution of 4.0 g. (0.01 mole) of **11** and 6.3 g. (0.13 mole) of dimethylamine in 50 ml. of benzene was kept at 25° for 24 hours in a stoppered flask, the whole warmed to 65°, cooled, 6.0 g. of dimethylamine in 25 ml. of benzene added, and the heating at 65° continued for an additional 4 hours. The mixture was filtered and the filtrate was extracted with 10% aqueous hydrochloric acid. The acid extracts were treated with an excess of aqueous sodium hydroxide and extracted with ether. Workup of the ether solution gave 2.7 g. (63% yield) of (I-19), m.p. 112-113° after recrystallization from petroleum ether; ν (mull) 2900 (broad, s), 1660 (s), 1460 (s), 1420 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.30-6.83 (m, 7 ar H), 6.20, 4.05 (A_2B_{2q}, J = 15, 2H, position-11), 4.50, 3.66 (A_2B_{2q}, J = 15, 2H, position-6), 2.68 (m, 2H, -C(=O)CH_2CH_2), 2.30 (t, 2H, -C(=O)-CH_2CH_2), 2.13 [s, 6H, -N(CH_3)$_2$].

12-[3-(Dimethylamino)propyl]-6,11-dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (I-6). Method E.

A solution of 5.0 g. (0.013 mole) of **11** in 200 ml. of anhydrous ether was added in 0.5 hour to 0.74 g. (0.019 mole) of lithium aluminum hydride in 75 ml. of anhydrous ether. Subsequently, the mixture was stirred and heated under reflux for 1 hour and then worked up to give 4.5 g. (90% yield) of an oil that was not distilled; analysis (Calcd. Cl, 9.53, Found: Cl, 9.64) and the absence of any carbonyl absorption in the ir spectrum confirmed its structure as 12-(3-chloropropyl)-6,11-dihydro-2-(trifluoromethyl)-12*H*-dibenzo[*b*,*f*][1,4]thiazocine (**12**). A solution of 2.5 g. (0.0067 mole) of **12**, and 2.5 g. of dimethylamine in 30 ml. of benzene, in a sealed tube, was heated for 24 hours at 100°, cooled, filtered, and the filtrate dissolved in 50 ml. of ether. When the ether solution was shaken with 20 ml. of 5% aqueous hydrochloric acid, a precipitate of crude *hydrochloride* separated. This was filtered, treated with aqueous sodium hydroxide and the crude *base* (see below), isolated *via* ether extraction, was treated with 0.63 g. (0.007 mole) of oxalic acid in 10 ml. of diisopropyl ether to give (I-6)·*oxalate*, **13**; the yield was 2.5 g. (78%) m.p. 193-195°, after recrystallization from 95% ethanol; ν (mull) 2830 (s), 2675-2320 (broad, m), 1630 (broad, s), 1480-1445 (broad, s) cm^{-1}; pmr (DMSO-d_6) δ 8.22 [s, 2H, ($COOH$)$_2$], 7.57-7.05 (m, 7 ar H), 4.52 (s, 2H, position-6), 4.46 (s, 2H, position-11), 3.28 (t, 2H,

$>NCH_2$), 2.98 [t, 2H, $CH_2N(CH_3)_2$], 1.78 (m, 2H $>NCH_2CH_2$), 2.59 (s, 6H of $>N(CH_3)_2$.

Method F.

The lithium aluminum hydride reduction was carried out as in Method E, with the exception that (I-19) replaced **11**. The yield of **13** was 78%; the m.p. and mixture m.p. with the product obtained by Method E showed no depression. Decomposition of 0.50 g. of **13** with aqueous sodium bicarbonate gave 0.35 g. (92% yield) of (I-6), m.p. 48-50°; ν (mull) 2900 (broad, s), 1480 (s), 1450 (s), 1350 (m), 1315 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.5-6.9 (m, 7 ar H), 4.59 (s, 2H, position-6), 4.32 (s, 2H, position-11), 3.24 (t, 2H, $>NCH_2$), 2.08 [m, 8H, $CH_2N(CH_3)_2$], 1.64 (m, 2H, $>NCH_2CH_2$).

The (I-6) recovered by the above procedure from 3.0 g. (0.0064 mole) of **13**, in 75 ml. of ether, was mixed with 20 ml. of 5% aqueous hydrochloric acid, the precipitated solid was filtered, dried, and recrystallized from 1.5% aqueous hydrochloric acid to give 2.5 g. (93% yield) of (I-6)·HCl·H_2O, sinters 132°, melts 148-150°; ν 3420 (s), 2670 (s), 2460 (m), 1650 (m), 1600 (m), 1480 (s) cm^{-1}.

12-(2-Diethylaminoethyl)-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]-thiazocine (I-2). Method G.

A mixture of 17.1 g. (0.075 mole) of **4**, 4.8 g. (0.1 mole) of 50% sodium hydride and 500 ml. of anhydrous xylene was stirred and heated under reflux for 2 hours, cooled, and 62.5 ml. (0.125 mole) of 2*M* 2-(diethylamino)ethyl chloride in xylene added in 1 hour. Subsequently, the stirring and heating under reflux was continued for 20 hours, the reaction mixture filtered hot, and the cooled filtrate extracted with 5% aqueous hydrochloric acid. The acid extracts were treated with an excess of 40% aqueous sodium hydroxide, the *base* isolated *via* ether extraction, and then distilled to give 13.9 g. (57% yield) of (I-2) as a viscous oil, b.p. 171-173° (0.5 mm). To 13.9 g. (0.043 mole) of (I-2) in 50 ml. of anhydrous acetone was added 10.0 ml. (0.039 mole) of 3.9 *N* ethereal hydrogen chloride. The precipitated solid, 14.0 g., m.p. 167-168°, was recrystallized from acetonitrile-ether to give 8.4 g. (59% yield) of the hydrochloride, m.p. 179-180°, ν (mull) 2560 (s), 2470 (s), 1585 (m), 1480 (s), 1460 (s), 1440 (s) 1400 (s) cm^{-1}.

2-Chloro-12-[2-(dimethylamino)ethyl]-6,11-dihydro-12*H*-dibenzo-[*b*,*f*][1,4]thiazocine (I-5). Method H.

To 7.5 g. (0.028 mole) of **4** in 125 ml. of anhydrous toluene was added in 0.25 hour, under nitrogen at 25°, 19.0 ml. of a 1.6 *N* solution of BuLi in hexane. Subsequently, the mixture was stirred for 0.25 hour at 25°, for 4 hours at 70-75°, cooled to 25°, and 5.5 g. (0.036 mole) of 2-(dimethylamino)ethyl bromide in 60 ml. of anhydrous toluene added. Additional stirring continued for 2 hours at 25° and 6 hours at 50-60°. Workup, as in Method E, gave 2.1 g. (20% yield) of (I-5), m.p. 74-75°, after recrystallization from ethanol; ν (mull) 1570 (s), 1540 (m), 1470 (s), 1460 (s), 1360 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.5-6.6 (m, 7 ar H), 4.57 (s, 2H, position-6), 4.30 (s, 2H, position-11), 3.72 (t, $>NCH_2CH_2$), 2.28 (t, $>NCH_2CH_2$), 1.02 (s, 6H of $N(CH_3)_2$.

Anal. Calcd. for $C_{18}H_{21}ClN_2S$: Cl, 10.64; N, 8.42; S, 9.62. Found: Cl, 10.68; N, 8.36; S, 9.78.

When ether solutions of 2.6 g. (0.0078 mole) of (I-5) and 1.2 g. (0.01 mole) of maleic acid were mixed at 10-15°, the salt first separated as an oil that crystallized spontaneously. This was filtered and recrystallized from 2-propanol to give 2.7 g. (73% yield) of the maleate salt, m.p. 123-125°; ν (mull) 1625 (s), 1570 (s), 1540 (s), 1470 (s), 1450 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.3-6.8 (m, 7 ar H), 6.23 (s, 2H, -CH=CH-), 4.40 (s, 2H, position-6), 4.26 (s, 2H, position-11), 3.59 (t, 2H, $>NCH_2CH_2$), 3.11 (t, 2H, $>NCH_2CH_2N$), 2.80 [2, 6H, $N(CH_3)_2$].

12-(3-Dimethylaminopropionyl)-6,11-dihydro-6*H*-dibenzo[*b*,*f*]-[1,4]thiazocine (I-17). Method I.

A mixture of 5.5 g. (0.025 mole) of **4**, 6.4 g. (0.05 mole) of 3-chloropropionyl chloride, and 100 ml. of anhydrous toluene was heated under reflux for 2 hours and concentrated to dryness *in vacuo*. The residual oil crystallized spontaneously and was recrystallized from Skellysolve E to give 7.0 g. of the 12-(3-chloropropionyl) derivative, **14**, m.p. 157-159°; ν (deuteriochloroform) 1645 (s), 1560 (m), 1490 (m), 1470 (s), 1440 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.27-6.85 (m, 8 ar H), 6.17, 4.07 (A_2B_{2q}, J = 15, 2H, position-11), 4.45, 3.70 (A_2B_{2q}, J = 13, 2H, position-6), 3.88 (t, 2H, $-CH_2Cl$), 2.57 (m, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2$).

Anal. Calcd. for $C_{17}H_{16}ClNOS$: Cl, 11.15; N, 4.41. Found: Cl, 11.13; N, 4.61.

A mixture of 7.0 g. (0.022 mole) of **14**, 3.5 g. of dimethylamine, and 100 ml. of toluene was heated in a sealed tube for 24 hours at 93°, cooled, the tubes opened, and filtered. The filtrate was concentrated to dryness *in vacuo* to give a solid, m.p. 134-136°. The m.p. was unchanged after recrystallization from Skellysolve E; the yield of (I-17) was 7.0 g. (97%); ν (deuteriochloroform) 1640 (s), 1585 (m), 1565 (m), 1490 (s), 1470 (s), 1455 (s), 1440 (s), 1435 (s), 1400 (s), 1395 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.30-6.83 (m, 8 ar H), 6.18, 4.07 (A_2B_{2q}, J = 15, 2H, position-11), 4.47, 3.68 (A_2B_{2q}, J = 13, 2H, position-6), 2.66 (m, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2$), 2.30 (t, 2H, $CH_2N(CH_3)_2$, 2.13 (s, 6H, $N(CH_3)_2$.

2-Chloro-12-[2-chloroacetyl]-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]-thiazocine, 15. Method J.

To 13.0 g. (0.05 mole) of **3** and 10.0 g. (0.1 mole) of triethylamine in 500 ml. of anhydrous toluene was added 11.0 g. (0.05 mole) of chloroacetyl chloride in 100 ml. of anhydrous toluene maintaining the temperature at 5 to 10°. Subsequently, the mixture was stirred for 2 hours at room temperature and 0.5 hour at 55°, cooled, filtered, and the filtrate concentrated *in vacuo*. The residue was recrystallized from hexane to give 10.5 g. (61% yield) of **15**, m.p. 148-150°; ν (mull) 3100 (m), 2890 (m), 1685 (s), 1575 (m), 1460 (s), 1400 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.34-6.87 (m, 7 ar H), 6.14, 4.37 (A_2B_{2q}, J = 15, 2H, position-11), 4.33-3.50 (m, 4H, 2H, position-6, 2H, $\overset{O}{\overset{\|}{C}}-CH_2Cl$).

Anal. Calcd. for $C_{16}H_{13}Cl_2NOS$: Cl: 20.96; N, 4.14; S, 9.46. Found: Cl, 20.59; N, 4.38; S, 9.51.

2-Chloro-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine-12-carboxamide (I-24). Method K.

To 4.0 g. (0.04 mole) of phosgene in 30 ml. of anhydrous toluene was added in 0.33 hour, with stirring, 5.3 g. (0.02 mole) of **7** and 4.0 g. (0.04 mole) of triethylamine in 175 ml. of anhydrous toluene, maintaining the temperature at 10-15°. Subsequently, the mixture was stirred for 2 hours at 20°, filtered, the filtrate concentrated *in vacuo*, the residue extracted with ether, and the ether extracts concentrated to give 3.0 g. (57% yield) of the 12-carbonyl chloride (**16**), m.p. 152-154°, after recrystallization from cyclohexane; ν (mull) 1710 (s), 1570 (m), 1525 (m), 1460 (s), 1405 (m) cm^{-1}; pmr (deuteriochloroform) δ 7.34-6.82 (7 ar H), 5.80, 4.34 (A_2B_{2q}, J = 15, 2H, position-11), 4.46, 3.78 (A_2B_{2q}, J = 13, 2H, position-6).

Anal. Calcd. for $C_{15}H_{11}Cl_2NOS$: Cl, 21.87, N, 4.32; S, 9.88. Found: Cl, 21.54; N, 4.47; S, 9.92.

The **16**, 3.6 g. (0.011 mole), and 50 ml. of 3.2 *N* absolute ethanolic ammonia were heated in a sealed tube for 30 hours at 120-125°. The cooled tube was opened and the reaction mixture concentrated *in vacuo*. The residue, 4.0 g., was washed with water, dried, and recrystallized from acetonitrile to give 1.8 g. (54% yield) of (I-24), m.p. 223-225° dec.; ν (mull) 3450 (m), 3260 (m), 3140 (s), 1675 (s), 1605 (s), 1450 (broad, 2), 1410 (s) cm^{-1}; pmr (pyridine-d_6) δ 7.49-6.81 (m, 7 ar H), 6.58 (broad s, 2H, NH_2, exchanged with deuterium oxide), 6.32, 4.51 (A_2B_{2q}, J = 15, 2H, position-11), 4.97, 3.85 (A_2B_{2q}, J = 12, 2H, position-6).

6,11-Dihydro-12*H*-dibenzo[*b,f*][1,4]thiazocine-12-carbonyl Chloride (**17**).

The procedure described for **16**, gave **17** in 70% yield, m.p. 144-145°, after recrystallization from cyclohexane; ν 1725 (s), 1470 (s), 1445 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.25-6.95 (m, 8 ar H), 5.80, 4.34 (A_2B_{2q}, J = 15, 2H, position-11), 4.46, 3.78 (A_2B_{2q}, J = 13, 2H, position-6).

Anal. Calcd. for $C_{15}H_{12}ClNOS$: Cl, 12.23; N, 4.83. Found: Cl, 12.14; N, 4.96.

6,11-Dihydro-2-(trifluoromethyl)-6*H*-dibenzo[*b,f*][1,4]thiazocine-12-carbonyl Chloride, (**18**).

The procedure described for **16** gave **18** in 83% yield, m.p. 157-159°, after recrystallization from cyclohexane, ν (mull) 1710 (s), 1450 (m), 1425 (m), 1320 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.48-6.82 (m, 7 ar H), 5.86, 4.38 [A_2B_{2q}, J = 15, 2H, position -11], 4.56, 3.86 (A_2B_{2q}, J = 13, 2H, position-6).

Anal. Calcd. for $C_{16}H_{11}ClF_3NOS$: Cl, 9.90; N, 3.91. Found: Cl, 9.84; N, 3.97.

6,11-Dihydro-12-(1-pyrrolidinylcarbonyl)-2-(trifluoromethyl)-12*H*-dibenzo[*b,f*][1,4]thiazocine (I-32). Method L.

To 5.3 g. (0.015 mole) of **18** in 100 ml. of anhydrous toluene was added 2.1 g. (0.03 mole) of pyrrolidine in 20 ml. of anhydrous toluene in 10 minutes at 20°. Subsequently, the mixture was heated under reflux for 2 hours, filtered, and the filtrate concentrated *in vacuo* to give 5.7 g. of solid, m.p. 182-184°. Recrystallization from acetonitrile gave 4.5 g. (76% yield) of (II-32), m.p. 185-186°; ν (mull) 1645 (s), 1480 (m), 1440 (m), 1370 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.40-7.0 (m, 8 ar H), 5.1 (broad m, 2H, position-11, 4.4 (broad m, 2H, position-6), 3.07 (m, 4H, positions -2 and -5 of pyrrolidinyl group), 1.7 (m, 4H, positions-3 and -4 of pyrrolidinyl group).

N-[3-(Diethylamino)propyl]-6,11-dihydro-12*H*-dibenzo[*b,f*][1,4-thiazocine-12-carboxamide Hydrochloride (I-31). Method M.

To 3.2 g. (0.025 mole) of *N,N*-diethylpropylenediamine in 75 ml. of anhydrous xylene was added, at 20°, 0.48 g. (0.02 mole) of 50% sodium hydride, and the whole heated under reflux for 1 hour, cooled to 30°, and 4.1 g. (0.014 mole) of **17** in 25 ml. of anhydrous xylene added in 10 minutes. Subsequently, the mixture was heated under reflux for 3.5 hours, cooled, and extracted with 50 ml. of 2.5% aqueous hydrochloric acid. The acid extract was adjusted to *p*H 10, and the oily base extracted into ether. The washed and dried ether solution was treated with ethereal hydrogen chloride to give 4.3 g. of solid, m.p. 182-188°. Successive recrystallizations from absolute ethanol-anhydrous ether and from 2-propanol gave 1.9 g. (33% yield) of (I-31). hydrochloride, m.p. 193-194° dec; ν (mull) 3350 (m), 1650 (s), 1500 (s), 1455 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.40-7.0 (m, 8 ar H), 5.99, 4.20 (A_2B_{2q}, J = 15, 2H, position-11), 4.63, 3.73 (A_2B_{2q}, J = 13, 2H, position-6), 4.71 (d, N*H*), 3.10 (m, 8H, NH-$CH_2CH_2CH_2$ and $N(CH_2CH_3)_2$, 2.1 (m, 2H, $NHCH_2CH_2$), 1.38 (t, 6H of $N(CH_2CH_3)_2$).

6,11-Dihydro-6*H*-dibenzo[*b,f*][1,4]thiazocine-12-carboxylic Acid, Ester with 2-(2-Piperidinoethoxy)ethanol (I-35). Method N.

To 2.4 g. (0.05 mole) of 50% sodium hydride in 50 ml. of anhydrous toluene was added, dropwise, 8.8 g. (0.057 mole) of 2-(2-piperidinoethoxy)ethanol in 25 ml. of anhydrous toluene in 0.5 hour; considerable foaming occurred during the addition. To this mixture was added 9.8 g. (0.034 mole) of **17** in 75 ml. of anhydrous toluene, the whole heated under reflux for 1 hour, cooled, filtered, and the filtrate extracted with 250 ml. of 5% aqueous hydrochloric acid. The acid extract was treated with an excess of solid potassium carbonate, the oil base isolated *via* ether extraction, and the ether solution concentrated. The residue crystallized when triturated with diisopropyl ether and was recrystallized from ligroin to give 4.3 g. of (I-35), m.p. 69-71°; ν (deuteriochloroform) 1690 (s), 1475 (s), 1440 (s), 1400 (s), cm^{-1}; pmr (deuteriochloroform) δ 7.30-6.96 (m, 8 ar H), 5.80 (d, 1H, position-11), 4.34 (m, 2H, position-6 plus 1H, position-11), [3.5 (m, 4H), 2.4 (m, 7H), 1.5 (m, 7H), total 18H of side chain].

12-(Diethylcarbamoyl)-6,11-dihydro-12*H*-dibenzo[*b,f*][1,4]thiazocine, (I-27).

To 4.4 g. (0.02 mole) of **4**, 100 ml. of anhydrous toluene, and 2.5 g. (0.025 mole) of triethylamine, at 20°, was added in 0.25 hour 2.6 g. (0.02 mole) of diethylcarbamoyl chloride, the whole stirred 0.25 hour at 20°, then for 7 hours at 110°. Workup gave 4.0 g. of crude product, m.p. 123-126°. Recrystallization from diisopropyl ether gave 3.1 g. (41% yield) of (I-27), m.p. 126-128°; ν (mull) 1640 (s), 1555 (m), 1485 (s), 1450 (m), 1410 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.40-6.75 (m, 8 ar H), 4.90 (broad s, 2H, position-11), 4.25 (broad s, 2H, position-6), 3.2 [q, J = 7, 4H of $(CH_2CH_3)_2$], 0.72 [t, J = 7, 6H of $(CH_2CH_3)_2$].

6,11-Dihydro-12*H*-dibenzo[*b,f*][1,4]thiazocine-12-carbonitrile (**19**).

To 3.5 g. (0.016 mole) of **4**, 1.5 g. (0.018 mole) of anhydrous sodium acetate, and 100 ml. of methanol, at 20°, was added a solution of 2.0 g. (0.02 mole) of cyanogen bromide in 20 ml. of methanol in 10 minutes. The mixture was stirred for 4 hours at room temperature, for 2 hours at 40-45°, and then concentrated to dryness *in vacuo*. The residue was treated with water, the insoluble material was dissolved in ether, the ether solution was washed, dried, and concentrated to give 3.5 g. of solid, m.p. 110-112°. Recrystallization from cyclohexane gave 2.1 g. (52% yield) of **19**, m.p. 113-115°; ν (mull) 2220 (s), 1480 (m), 1470 (s), 1450 (m), 1440 (m), 1370 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.6-7.1 (m, 8 ar H), 5.0 (s, 2H, position-11), 4.3 (s, 2H, position-6).

Anal. Calcd. for $C_{15}H_{12}N_2S$: C, 71.39; H, 4.80; N, 11.09. Found: C, 71.35; H, 4.87; N, 11.11.

6,11-Dihydrothio-12*H*-dibenzo[*b,f*][1,4]thiazocine-12-carboxamide, (I-26).

To 5.7 g. (0.025 mole) of **4**, 3.8 g. (0.03 mole) of triethylamine, and 75 ml. of anhydrous toluene, at 0 to 5°, was added 3.5 g. (0.03 mole) of thiophosgene in 50 ml. of anhydrous toluene. The stirring was continued for 10 minutes at 0° and 4 hours at 20°, filtered, and the filtrate concentrated *in vacuo* to give 7.0 g. of solid. Recrystallization from cyclohexane gave 5.1 g. (67% yield) of the thiocarbamoyl chloride, **20**, m.p. 155-157° dec.; ν (mull) 1492 (m), 1472 (s), 1460 (s), 1440 (s), 1420 (s) cm^{-1}; pmr

(deuteriochloroform) δ 7.35-6.90 (m, 8 ar H), 6.67, 4.50 (A_2B_{2q}, J = 15, 2H, position-11), 4.80, 3.80 (A_2B_{2q}, J = 13, 2H; position-6).

Anal. Calcd. for $C_{15}H_{12}ClNS_2$: Cl, 11.56; S, 20.97. Found: Cl, 11.76; S, 20.97.

A suspension of 2.0 g. (0.0065 mole) of **20** and 50 ml. of 3.5 *N* ethanolic ammonia was stirred in a stoppered flask at room temperature for 60 hours and then worked up to give 0.6 g. (33% yield) of (I-26), m.p. 239-241° dec., after recrystallization from benzene; ν (mull) 3440 (s), 3270 (s), 3160 (s), 1610 (s), 1470 (s), 1460 (s), 1440 (s), 1380 (s) cm^{-1}; pmr (deuteriochloroform) δ 7.25-6.9 (m, 8 ar H), 6.75, 4.36 (A_2B_{2q}, J = 15, 2H, position-11), 5.47 (2H, NH_2), 4.70, 3.65 (A_2B_{2q}, J = 12, 2H, position-6).

12,12'-Carbonyl bis[12*H*-dibenzo[*b*,*f*][1,4]thiazocin-11(12*H*)-one] (**21**).

To a suspension of 1.1 g. (0.02 mole) of 50% sodium hydride in 200 ml. of anhydrous toluene was added, in portions, a total of 4.8 g. (0.02 mole) of 12*H*-dibenzo[*b*,*f*][1,4]thiazocin-11(12*H*)-one (8). The mixture was stirred for 3 hours at 20°, 1.0 g. (0.01 mole) of phosgene in 9 ml. of anhydrous toluene was added in 0.5 hour, and the whole was kept 18 hours at room temperature, heated for 2 hours at 75-80°, cooled, and the insoluble material filtered (Solid A). The filtrate was concentrated *in vacuo* and gave a residue (Solid B). Solid A, 1.5 g., melted at 205-208° while Solid B, 3.7 g., melted at 205-210°. The solids were combined, washed with 25 ml. of ether and recrystallized repeatedly from ethyl acetate to give 1.6 g. (32% yield) of **21**, m.p. 244-246°; ν (mull) 1700 (s), 1600 (m), 1475 (m), 1450 (m), 1430 (m) cm^{-1}; (deuteriopyridine) δ 7.88-6.67 (16 ar H), 5.43, 5.22 (A_2B_{2q}, J = 4, 2H, position-6 of one tricycle), 4.11, 3.88 (A_2B_{2q}, J = 7, 2H, position-6 of the other tricycle).

Anal. Calcd. for $C_{29}H_{20}N_2O_3S_2$: C, 68.45; H, 3.96; N, 5.50; S, 12.60. Found: C, 68.51; H, 3.88; N, 5.76; S, 12.63.

A Dreiding model of **21** revealed that the rigidity of the carbonyl oxygen linkage has imposed an asymmetry to the molecule. Thus, if planes are drawn through each tricyclic system so that a benzene ring and a sulfur atom occupy each plane, the planes are not parallel, and one nitrogen atom occupies a position approximately 1.8 Å below the other nitrogen atom and the methylene groups are about 4.4 and 5.4 Å from the common carbonyl oxygen atom. It is not unexpected, therefore, that the signals of these methylene groups in the pmr spectrum would show a non-equivalency.

12-Benzyl-6,11-dihydro-12*H*-dibenzo[*b*,*f*][1,4]thiazocine, (**22**).

To 1.25 g. (0.0055 mole) of **4**, 2.3 g. (0.012 mole) of benzyl bromide, and 50 ml. of anhydrous tetrahydrofuran was added in small increments a total of 0.58 g. (0.012 mole) of 50% sodium hydride. The mixture was stirred for 72 hours at 20°, filtered, and the filtrate concentrated *in vacuo*. The residue was worked up to give 0.25 g. (14% yield) of **22**, m.p. 97-99°; ν (deuteriochloroform) no NH, 1580 (m), 1490 (m), 1475 (s), 1450 (s), 1425 (m) cm^{-1}; pmr (deuteriochloroform) δ 7.35-6.95 (m, 13 ar H), 4.68 (s, 2H, position-6), 4.36 (s, 4H,. 2H, position-11, 2H, position-12).

Anal. Calcd. for $C_{21}H_{19}NS$: C, 79.45; H, 6.03; N, 4.43; S, 10.10. Found: C, 79.85; H, 6.09; N, 4.42; S, 10.06.

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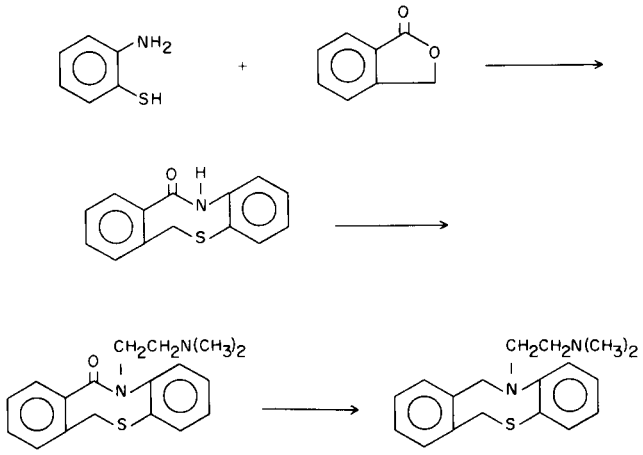

alkylated product reduced to **24**. We prepared **23** by the procedure described in the above patent and are reporting its spectral properties for the first time: ν (mull) 3140 (broad, w), 1665 (s), 1468 (m), 1452 (m) cm^{-1}; pmr (deuteriopyridine) 7.48-7.10 (m, 8 ar H), 4.57, 4.00 (A_2B_{2q}, J = 13, 2H, position-6).

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(10) The authors are indebted to Dr. J. Z. Gougoutas of the Department of Chemistry, University of Minnesota and Mrs. Barbara Toeplitz of the Squibb Institute for Medical Research for this section of the paper and the x-ray crystallographic studies reported therein. A more detailed comparison of the two molecular conformations will be presented in a separate paper after additional refinements have been completed.

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