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A considerable number of new tri and tetracyclic heterocycles (II) and open chain intermediates were synthesized. These were tested in a battery of assays designed to reveal central nervous system (CNS) activity. However, none showed useful activity greater than known analogs.

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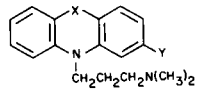
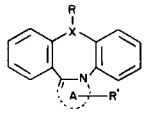
Certain amino-alkyl tricyclic heterocycles (*e.g.*, Ia and b) are well known as central nervous system depressants or antidepressants. In these laboratories it was found that certain analogous tetracycles also possessed depressant or



Ia, X = S, Y = Cl, Chlorpromazine

Ib, X = CH_2CH_2, Y = H, Imipramine

antidepressant properties (2,3). In following up these leads a considerable number of new tetracycles of type II were prepared and are listed in Table I. Ring A was a variety of



II

five and six-membered rings, X was carbon, sulfur or nitrogen. In many cases R or R' was a dimethylaminoalkyl chain analogous to that in I. Also in Table I are a variety of tetracycles made as possible intermediates. These compounds were prepared by a variety of methods involving ring closure of the A ring and are described in the Experimental along with a number of new open chain and tricyclic compounds also desired as intermediates.

Most of these compounds were screened in mice by a battery of tests (4) designed to pick up useful CNS active drugs. However, none were more active than the lead compounds (2,3).

EXEPERIMENTAL (5)

Methyl 2'-Benzylsuccinanilate (**1**).

To a cold solution of 5.5 g. (0.03 mole) of 2-benzylaniline and 4.7 ml. (0.06 mole) of pyridine in 100 ml. of tetrahydrofuran was added dropwise 5.42 g. (0.036 mole) of 3-carbomethoxypropionyl chloride. After stirring, under nitrogen, at 0° for 15 minutes and at room temperature for 19 hours the mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was chromatographed on silica gel eluting with 5% ethyl acetate in hexane. The product was crystallized from acetone-hexane yielding 5.05 g. (57%) of fluffy white needles, m.p. 94-96°. Ir, nmr, and ms support the structure.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.17. Found: C, 72.65; H, 6.41; N, 4.65.

N-(α-Phenyl-*o*-tolyl)succinimide (**2**).

A solution of 1.56 g. (0.01 mole) of 2-benzylaniline in 25 ml. of 2,2'-dimethoxydiethyl ether, under nitrogen, was refluxed for 18 hours, cooled and poured over ice. The product was extracted with chloroform, washed with water, dried over sodium sulfate, and evaporated. The residue was crystallized from ethyl acetate yielding 1.7 g. (62%) of colorless needles, m.p. 141.5° dec. Ir, nmr and ms support the structure.

Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.01; H, 5.87; N, 5.10.

9,13b-Dihydro-3*H*-dibenzo[*c,f*]pyrrolo[1,2-*a*]azepin-3-one (**3**).

A mixture of 30 g. of **2**, 40 ml. of phosphoryl chloride, and 200 ml. of polyphosphoric acid was stirred vigorously, under nitrogen, at 105° for 18 hours. After cooling, ice water was added and the mixture was extracted with chloroform. The extract was washed with water, saturated sodium chloride solution, and dried over sodium sulfate. After filtration and evaporation the product was crystallized from ethyl acetate yielding 7.56 g. (28%) of pale green crystals, m.p. 160° dec.; ir (Nujol): 3600, 3510 (NH/OH, probably water), 1710, 1695 (C=O), 1630 (C=C, possibly water), 1600, 1490 (C=C), 1355, 1315 (C-N/C-C), 765, 750, 740, 720 (arom.) cm^{-1}; nmr (deuteriochloroform): δ about 1.7 (broad, possibly water), 3.38 (d, 2, CH_2CO), AB centered at 3.37 and 4.3 (2, J = 13.5 Hz, CH_2), 5.44 (t, 1, =CH), between 7.05 and 7.7 (m, 8, arom. H's); ms: M^+ 247.

8*H*-Dibenzo[*c,f*]-*v*-triazolo[1,5-*a*]azepine (**4**).

A mixture of 17.4 g. (0.084 mole) of 6-methylmorphanthridine (6) and 16.4 g. (0.16 mole) of benzenesulfonylazide in a one l. round bottomed flask (to contain foaming), equipped with stirrer and condenser, was heated, under nitrogen, at 116° for 24 hours. The resultant black mixture was sublimed in several portions at 153° under high vacuum giving 16.1 g. of a mixture of benzenesulfonamide and the product. These were separated by chromatography on 700 g. of silica gel eluting with 3% methanol in chloroform. The product was recrystallized from benzene-ether yielding 3.4 g. (17%) of white crystals, m.p. 124.5-127°. Ir, nmr, and ms support the structure.

8*H*-Dibenzo[*c,f*]-*v*-triazolo[1,5-2]azepin-8-one (**5**).

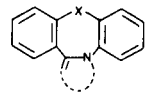
A mixture of 14 g. (0.06 mole) of 4 and 50 ml. of acetic acid was treated with 30 ml. of 2.7 *M* aqueous chromic acid solution and stirred on a steam bath for 2 hours during which an additional 30 ml. of chromic acid solution was added dropwise. The thick mixture was poured into 400 ml. of ice-cold 7% aqueous sodium hydroxide and extracted with chloroform. The chloroform solution was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The residue was crystallized from ethyl acetate yielding 9.7 g. (65.4%) of white crystals, m.p. 236-238°; ir (Nujol): 3110 (=CH), 1660 (C=O), 1600, 1490 (C=C/C=N/N=N), 1310, 1285, 930 (C-N/other), 755 (arom.) cm^{-1}; nmr (deuteriochloroform) only aromatic H's between δ 7.2 and 8.4; ms M^+ 247.

8-[3-(Dimethylamino)propyl]-8*H*-dibenzo[*c,f*]-*v*-triazolo[1,5-*a*]acepin-8-ol (**6**).

3-(Dimethylamino)propylmagnesium chloride was prepared from 0.145 g. (0.006 g. atom) of magnesium, 1.7 ml. of a benzene solution containing

0022-152X/80/020341-10$02.25

Table I



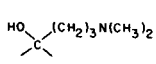
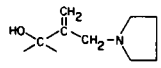
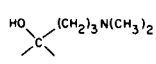
Compound No.	X		Formula	Analysis (a) C	H	N
3			$C_{17}H_{13}NO$	81.51 (b) (82.57)	5.57 (5.30)	5.75 (5.66)
4			$C_{15}H_{11}N_3$	77.50 (77.23)	5.02 (6.75)	17.81 (18.01)
5			$C_{25}H_9N_3O$	72.42 (72.86)	3.69 (3.67)	17.06 (17.00)
6			$C_{20}H_{22}N_4O$	71.69 (71.83)	6.62 (6.63)	16.88 (16.75)
7			$C_{22}H_{22}N_4O$	73.31 (73.72)	6.36 (6.16)	15.42 (15.63)
8			$C_{16}H_{13}N_3O$	72.60 (72.99)	4.96 (4.98)	15.83 (15.95)
9			$C_{15}H_9N_3O$	72.60 (72.86)	3.63 (3.67)	17.08 (17.00)
10			$C_{20}H_{22}N_4O$	71.89 (71.83)	6.61 (6.63)	16.66 (16.75)
12			$C_{20}H_{26}N_2O_3$	72.17 (72.28)	4.94 (4.85)	8.49 (8.43)
13			$C_{20}H_{16}N_2O_3$	72.31 (72.28)	4.73 (4.85)	8.34 (8.43)
14			$C_{16}H_{12}N_2O_3$	71.26 (71.04)	3.86 (3.98)	9.47 (9.20)
15			$C_{22}H_{21}N_3O_3$	70.45 (70.38)	5.58 (5.64)	11.17 (11.19)
16			$C_{22}H_{22}N_4O_2$	70.35 (70.57)	5.89 (5.92)	14.83 (14.96)
17			$C_{18}H_{14}N_4O_2$	67.73 (67.91)	4.53 (4.43)	17.38 (17.60)
18			$C_{20}H_{16}N_2O_2S$ (c)	68.54 (68.94)	4.72 (4.63)	8.07 (8.04)
19			$C_{19}H_{16}N_2O_2$	74.99 (74.98)	5.34 (5.30)	9.28 (9.20)
22			$C_{19}H_{14}N_2O_3S$ (d)	64.91 (65.13)	4.10 (4.03)	8.12 (7.99)

Table I continued

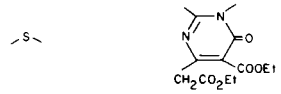
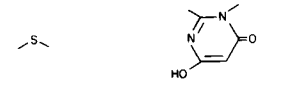
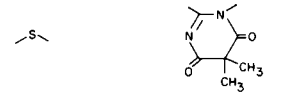
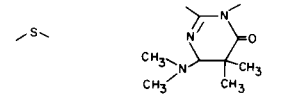
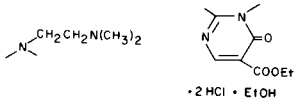
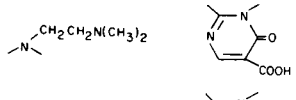
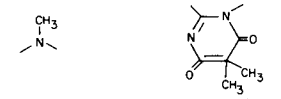
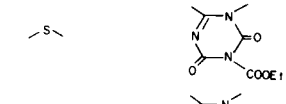
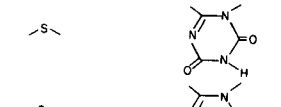
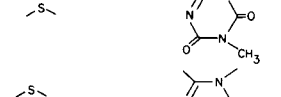
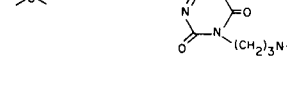
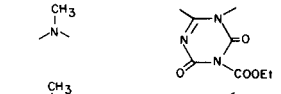
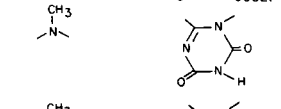
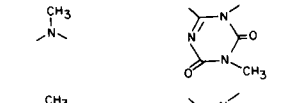
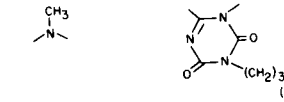
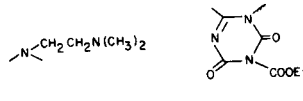
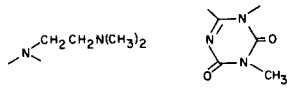
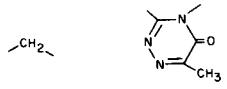
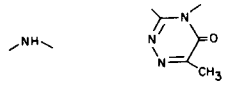
Compound No		Formula	Analysis (a) C	H	N
24		$C_{23}H_{20}N_2O_5S$ (e)	63.68 (63.29)	4.75 (4.62)	6.26 (6.42)
25		$C_{29}H_{20}N_4O_2S_2$ (f)	66.97 (66.90)	4.20 (3.87)	10.37 (10.76)
26		$C_{16}H_{10}N_2O_2S$ (g)	64.93 (65.29)	3.43 (3.42)	9.30 (9.52)
27		$C_{18}H_{14}N_2O_2S$ (h)	66.80 (67.06)	4.62 (4.38)	8.35 (8.69)
28		$C_{20}H_{21}N_3OS$ (i)	68.36 (68.36)	6.07 (6.02)	11.92 (11.96)
34		$C_{23}H_{26}Cl_2N_4O_3$ $\cdot C_2H_5OH$ (j)	56.72 (57.36)	6.28 (6.16)	10.41 (10.70)
35		$C_{21}H_{21}ClN_4O_3$ $\cdot H_2O$ (k)	58.59 (58.54)	5.04 (5.38)	12.82 (13.00)
36		$C_{19}H_{17}N_3O_2$	71.60 (71.45)	5.71 (5.37)	13.03 (13.16)
38		$C_{18}H_{13}N_2O_4S$ (l)	59.04 (58.85)	3.70 (3.57)	11.48 (11.44)
39		$C_{15}H_9N_3O_2S$ (m)	61.08 (61.00)	3.47 (3.07)	14.34 (14.23)
40		$C_{16}H_{11}N_3O_2S$ (n)	61.96 (62.12)	3.75 (3.59)	13.45 (13.58)
41		$C_{20}H_{20}N_4O_2S$ (o)	62.90 (63.13)	5.20 (5.30)	14.80 (14.73)
42		$C_{19}H_{16}N_4O_4$	62.95 (62.63)	4.68 (4.43)	15.71 (15.38)
43		$C_{16}H_{12}N_4O_2$	65.67 (65.74)	4.31 (4.14)	19.30 (19.17)
44		$C_{17}H_{14}N_4O_2$	66.75 (66.65)	4.69 (4.61)	18.50 (18.29)
45		$C_{21}H_{23}N_5O_2$	66.68 (66.82)	6.35 (6.14)	18.30 (18.56)
46		$C_{22}H_{23}N_5O_4$ (p)	—	—	—

Table I continued

Compound No.		Formula	Analysis (a) C	H	N
48		$C_{20}H_{21}N_5O_2$	65.92 (66.10)	5.92 (5.83)	19.09 (19.27)
50		$C_{17}H_{13}N_3O$	74.11 (74.17)	4.82 (4.76)	15.25 (15.26)
51		$C_{16}H_{12}N_4O$ ·0.145 EtOAc ·0.06 CH_2Cl_2 (q)	68.49 (68.06)	4.47 (4.56)	19.46 (19.07)

(a) Figures in parentheses are calculated values. (b) The low carbon analysis may be explained by presence of water as indicated by ir and nmr. (c) Calcd.: S, 9.20; Found: 9.04. (d) Calcd.: S, 9.15. Found: 8.97. (e) Calcd.: S, 7.34. Found: 7.35. (f) Salt of **26** with 11-aminodibenzo[*b*,*f*][1,4]-thiazepine. Calcd.: S, 12.32. Found: 12.04. (g) Calcd.: S, 10.89. Found: 11.11. (h) Calcd.: S, 9.95. Found: 10.30. (i) Calcd.: S, 9.10. Found: 9.45. (j) Calcd. for the dihydrochloride-ethanol solvate: Cl, 13.55. Found: 13.02. (k) Calcd. for the hydrochloride-hydrate: Cl, 8.23; H_2O 4.18. Found: Cl, 8.16; H_2O (K.F.) 5.57. (l) Calcd.: S, 8.73. Found: 8.83. (m) Calcd.: S, 10.85. Found: 10.63. (n) Calcd.: S, 10.36. Found: 10.18. (o) Calcd.: S, 8.43. Found: 8.66. (p) Previously reported (3) but in much poorer yield. (q) Found by melt solvate: 4.20% ethyl acetate and 1.72% methylene chloride. The calculated values for C, H, and N take this into account.

0.006 mole of 3-(dimethylamino)propyl chloride, 5 ml. of tetrahydrofuran, and 3 drops of 1,2-dibromoethane. Then a suspension of 0.74 g. (0.003 mole) of **5**, in 15 ml. of tetrahydrofuran was added and the mixture was stirred at room temperature for 3 hours. After distilling off most of the solvent the mixture was cooled and 10 ml. of saturated aqueous ammonium chloride was added. The mixture was well extracted with ether, the extract was washed with water, and evaporated. The residue was crystallized from ethyl acetate-hexane yielding 0.29 g. (29%) of white crystals, m.p. 122-124°. Ir, nmr, and ms support the structure.

8-[1-(1-Pyrrolidinylmethyl)vinyl]-8*H*-dibenzo[*c*,*f*]-*v*-triazolo[1,5-*a*]azepin-8-ol (**7**).

1-(1-Pyrrolidinylmethyl)vinylmagnesium bromide was prepared from 0.435 g. (0.018 g.-atom) of magnesium, 3.42 g. (0.018 mole) of 2-bromo-3-(1-pyrrolidinyl)propene, and 15 ml. of tetrahydrofuran. The reaction was started by the addition on a small crystal of iodine. After refluxing for one hour, 2.22 g. (0.009 mole) of solid **5** and 10 ml. more tetrahydrofuran were added and the mixture was stirred under reflux for 2 hours. Part of the solvent was distilled off and 40 ml. of saturated ammonium chloride was added. The mixture was extracted with ether and the extract was washed with water and evaporated. The residue was crystallized from ethyl acetate yielding 1.8 g. (56-60%) of white crystals, m.p. 164-166°. Ir and ms confirmed the structure.

2,9-Dihydro-2-methyl-3*H*-dibenzo[*c*,*f*]-*s*-triazolo[4,3-*a*]azepin-3-one (**8**).

A solution of 2.28 g. (0.01 mole) of 6-chloromorphanthridine (7) and 1.42 g. (0.12 mole) of ethyl 2-methylcarbazate in 25 ml. of ethanol was stirred at room temperature under nitrogen for 18 hours and then at reflux for 6 hours. The solvent was evaporated *in vacuo* and the residue was mixed with 60 ml. of 1 *N* hydrochloric acid and filtered. The solid was dissolved in chloroform, washed with water, cold 5% sodium hydroxide, again with water. The solution was evaporated *in vacuo* and the residue was recrystallized repeatedly from 2-propanol yielding 0.88 g. (30%) of white needles, m.p. 203-204°. Ir, uv, nmr, and ms support the structure.

9*H*-Dibenzo[*c*,*f*]-*s*-triazolo[4,3-*a*]azepin-9-one (**9**).

A solution of 4.6 g. (0.02 mole) of 9*H*-dibenzo[*c*,*f*]-*s*-triazolo[4,3-*a*]azepine (8) in 50 ml. of acetic acid was treated dropwise, under nitrogen, with stirring with 20 ml. of 2.7 *M* aqueous chromic acid solution. The solution was then refluxed for 3 hours, cooled, and poured into 500 ml. of ice-cold 5% potassium hydroxide. The product was extracted with chloroform, washed with water, and dried over sodium sulfate. After evaporation *in vacuo* the residue was triturated with 40 ml. of hot ethyl acetate and collected on a filter, yielding 4.0 g. (82%) of white prisms, m.p. 293-294°. Ir and ms support the structure.

9-[3-(Dimethylamino)propyl]-9*H*-dibenzo[*c*,*f*]-*s*-triazolo[4,3-*a*]azepin-9-ol (**10**).

This was prepared by the procedure described above for **6** from 0.74 g. (0.003 mole) of **9**. The product was crystallized from ethyl acetate yielding 0.32 g. (32%) of white crystals, m.p. 191-193°. Ir, nmr and ms support the structure and differ as expected from the isomeric **6**.

Diethyl [(6-Morphanthridinylamino)methylene]malonate (**11**).

A mixture of 2.08 g. (0.01 mole) of 6-aminomorphanthridine (3) and 2.6 g. (0.012 mole) of diethyl ethoxymethylenemalonate was stirred under nitrogen at 100° for 2 hours. After cooling the product was dissolved in 100 ml. of hot cyclohexane, filtered, and concentrated to 35 ml. On cooling 3.11 g. (82%) of white crystals was obtained, m.p. 130-132°. Recrystallization from 30 ml. of 2-propanol yielded 2.63 g. of crystals, m.p. 131-132.5°. Tlc (silica gel, 5% methanol in chloroform) showed only one spot; ir (Nujol): 3240 (NH), 1710, 1670 (C=O), 1640, 1605, 1585, 1565, (C=O/C=N), 1345, 1290, 1275, 1225, 1085, 1060, 1030 (C-O/C-N), 800, 770 (arom) cm^{-1}; nmr (deuteriochloroform): δ 1.37 (t, 6, CH_2CH_3), 3.67 (s, 2, Ph_2CH_2), 4.33 (q, 4, CH_2CH_3), between 7.0 and 7.7 (m, 8, arom H's), 9.27 (d, 1, CH=C), 11.1 (broad d, 1, NH).

Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.48; H, 5.79; N, 7.40.

Ethyl 4,10-Dihydro-4-oxodibenzo[*c*,*f*]pyrimido[1,2-*a*]azepine-3-carboxylate (**12**), and Ethyl 2,10-Dihydro-2-oxodibenzo[*c*,*f*]pyrimido[1,2-*a*]azepine-3-carboxylate (**13**).

A solution of 10.4 g. (0.05 mole) of 6-aminomorphanthridine (3) and 13 g. (0.06 mole) of diethyl ethoxymethylenemalonate in 60 ml. of 1,2,4-trichlorobenzene was heated, under nitrogen, at 100° for 1 hour and then refluxed under a short air condenser for 3 hours. After concentrating *in vacuo* the solution was diluted with pentane giving 14.9 g. of light brown solid. This was dissolved in 450 ml. of ethanol, treated hot with decolorizing charcoal, filtered, and concentrated to 250 ml. Cooling gave 10.5. g. of cream colored crystals, m.p. 183.5-185° which was assigned the structure **12** on the basis of physical properties, especially ir which showed a higher carbonyl absorption than **13** (below) expected for the mono conjugated carbonyl, ir (Nujol): 1745 (ester C=O), 1705 (ring C=O), 1675 (C=O/C=C/C=N), 1600, 1585, 1570, 1505 (C=C/C=N), 1305, 1270, 1115, 1108 (C-O/other), 805, 780, 775 (arom.) cm^{-1}; nmr (deuteriochloroform): δ

1.38 (t, 3, CH_2CH_3), AB centered at 3.57 and 4.52 (2, J = 13 Hz, Ph_2CH_2), 4.39 (q, 2, CH_2CH_2), between 7.0 and 8.1 (m, 8, arom. H's), 8.8 (s, 1, CH=C); uv max (ethanol): 270 mμ (ε 7,200), 340 (12,850); ms: M^+ 332.

On standing in an open flask the filtrate from **12** deposited a mixture of white and yellow crystals. About 0.2 g. of the yellow crystals were picked out and recrystallized from ethanol giving 0.16 g. of pale yellow crystals, m.p. 257-258°. Tlc (silica gel, 5% methanol in chloroform) showed one spot, different from **12** above. This was assigned structure **13** on the basis of physical properties, especially ir (see above); ir (Nujol): 1735 (ester C=O), 1640 (ring C=O), 1600, 1585, 1505 (C=C/C=N), 1415, 1350, 1240, 1095 (C-O/C-N/other), 775 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.38 (t, 3, CH_2CH_3), AB centered at 3.70 and 4.25 (2, J = 13 Hz, Ph_2CH_2), 4.40 (q, 2, CH_2CH_3), between 7.1 and 8.2 (m, 8, arom H's), 8.43 (s, 1, CH=C); uv max (ethanol): 257 mμ (ε 30,900); ms: M^+ 332.

4,10-Dihydro-4-oxodibenzo[*c,f*]pyrimdio[1,2-*a*]azepine-3-carboxylic Acid (**14**).

To a solution of 3.32 g. (0.01 mole) of **12** in 100 ml. of tetrahydrofuran, under nitrogen, was added 20 ml. of 20% aqueous sodium hydroxide. The mixture was stirred at room temperature and became very thick. After 24 hours the mixture was diluted with 1 l. of water and extracted with ether. The aqueous solution was acidified with hydrochloric acid giving a gum which soon crystallized. The product was collected, washed with water, and dried giving 2.8 g. of yellow solid. Recrystallization from 250 ml. of methanol yielded 2.4 g. (80%) of tan crystals, m.p. 253.5-255.5° dec. Ir, nmr, and ms support the structure.

2-(Dimethylamino)ethyl 4,10-Dihydro-4-oxodibenzo[*c,f*]pyrimido[1,2-*a*]-azepine-3-carboxylate (**15**).

A mixture of 1.66 g. (0.005 mole) of (**12**), 20.6 ml. (0.2 mole) of 2-(dimethylamino)ethanol in which a small piece of sodium was dissolved, and 100 ml. of toluene, under nitrogen, was stirred at the boiling point for 1 hour. After cooling the mixture was diluted with water and extracted with ether. The ether extract was washed with water and evaporated giving a solid which was recrystallized from 2-propanol yielding 0.45 g. (24%) of yellow-tan crystals, m.p. 160-162.5°. Ir, nmr, and ms support the structure.

The above aqueous solution containing gelatinous solid was acidified and the solid recrystallized from methanol giving a 46% recovery of starting material as the free acid **14**.

N-[2-(Dimethylamino)ethyl]-4,10-dihydrodibenzo[*c,f*]pyrimido[1,2-*a*]azepine-3-carboxamide (**16**).

To a solution of 2.43 g. (0.008 mole) of **14**, in 50 ml. of tetrahydrofuran, under nitrogen, was added with stirring at room temperature, 1.6 g. (0.01 mole) of 1,1'-carbonyldiimidazol. The mixture was stirred under reflux for 0.5 hour, cooled to 0° and 1.15 ml. (0.01 mole) of *N,N*-dimethyl-1,2-ethanediamine was added dropwise. After stirring at 0° for 0.5 hour and at room temperature overnight the resulting solid was collected, washed with tetrahydrofuran and dried giving 2.43 g. of white solid, m.p. 232-234°. An additional 0.4 g. of slightly less pure product was obtained from the filtrate. The combined product was dissolved in 150 ml. of ethanol and 50 ml. of methylene chloride, filtered, concentrated and cooled, yielding 2.57 g. (86%) of white crystals, m.p. 231.5-234°. Ir and nmr support the structure.

4,10-Dihydro-4-oxodibenzo[*c,f*]pyrimido[1,2-*a*]azepine-3-carboxylic Acid Hydrazide (**17**).

A solution of 1.66 g. (0.005 mole) of **12** and 3.0 ml. (0.06 mole) of hydrazine hydrate in 50 ml. of ethanol, under nitrogen, was stirred under reflux for 6.5 hours and evaporated *in vacuo*. The residue was dissolved in 75 ml. of methanol, filtered, concentrated to 30 ml. and cooled giving 0.65 g. (41%) of bright yellow crystals, m.p. 220-221.5° dec.; ir (Nujol): 3320 (NH), 1680 (C=O), 1600, 1590, 1565, 1535, 1495 (C=C/C=N/other), 1200, 960 (other), 770 (arom.) cm^{-1}; nmr (deuteriochloroform + deuterium oxide): AB centered at δ 3.63 and 4.05 (2, J = 13 Hz, Ph_2CH_2), between 7.1 and 8.15 (m, 8, arom. H's); ms: M^+ 318.

Ethyl 4,10-Dihydro-4-thioxodibenzo[*c,f*]pyrimido[1,2-*a*]azepine-3-carboxylate (**18**).

A mixture of 3.32 g. (0.01 mole) of **12**, 150 ml. of toluene, and 4.5 g. (0.02 mole) of phosphorus pentasulfide was stirred under reflux, under nitrogen, for 12 hours. An additional 2.25 g. (0.01 mole of phosphorus pentasulfide was added and refluxing was continued for 12 hours more. The mixture was filtered and the solid was extracted with methylene chloride. The combined toluene and methylene chloride solution was washed with aqueous sodium bicarbonate, water, and evaporated *in vacuo*. The residue was chromatographed on silica gel eluting with 20% ethyl acetate in hexane giving 2.1 g. (60%) of **18**. A sample was recrystallized from 2-propanol, m.p. 158-160°. Ir and ms support the structure.

3,3-Dimethyldibenzo[*c,f*]pyrimido[1,2-*a*]azepine-2,4(3*H*,10*H*)dione (**19**).

A solution of 2.08 g. (0.01 mole) of 6-aminomorphanthridine and 2.33 ml. (0.024 mole) of triethylamine in 50 ml. of tetrahydrofuran was cooled to 0° under nitrogen and 1.44 ml. (0.011 mole) of dimethylmalonyl dichloride was added. After stirring at 0° for 2 hours the mixture was evaporated *in vacuo*. The residue was shaken with a mixture of cold dilute hydrochloric acid and ether and filtered. The solid was washed with water and ether and dried giving 2.3 g. (76%) of white solid, m.p. 233-234.5°. Recrystallization from ethanol yielded 1.64 g. of white crystals, m.p. 235-237°. Ir, nmr, and ms support the structure.

2-Methyl-*N*-(6-morphanthiadinyl)propionamide (**20**).

In another attempt to prepare **19**, the amide **20** was obtained instead, undoubtedly by decarboxylation of the intermediate dimethylmalonic acid monoimidazolide.

To a solution of 3.24 g. (0.02 mole) of 1,1'-carbonyldiimidazole in 10 ml. of tetrahydrofuran was added a solution of 1.32 g. (0.01 mole) of dimethylmalonic acid in 10 ml. of tetrahydrofuran. After stirring for 30 minutes at room temperature a solution of 2.08 g. (0.01 mole) of 6-aminomorphanthridine (3) in 10 ml. of tetrahydrofuran was added and the mixture was stirred for 3 hours. After removal of the solvent *in vacuo* the residue was chromatographed on silica gel, eluting with 3% methanol in chloroform. The product was recrystallized from 2-propanol yielding 0.43 g. (16%) of crystals, m.p. 153-154°; ir (Nujol): 3230 (NH), 1675, 1615, 1595, 1565, 1515, 1490 (C=O/C=N/C=C), 1320, 1290, 1205 (C-N/C-O/other), 775, 770, 735 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.20 and 1.32 (two s's, 6, two CH_3's), 2.79 (m, 1 CH), 3.79 (s, 2, Ph_2CH_2), between 7.0 and 7.5 (m, 8, arom. H's), 7.72 (broad s, 1, NH); ms: M^+ 278.

Diethyl [(Dibenzo[*b,f*][1,4]thiazepin-11-yl-amino)methylene]malonate (**21**).

A mixture of 4.53 g. (0.02 mole) of 11-aminobenzo[*b,f*][1,4]thiazepine (9) and 4.83 ml. (0.024 mole) of diethyl ethoxymethylenemalonate was heated, under nitrogen, with stirring at 100° for 2 hours. The mixture was dissolved in 75 ml. of hot 2-propanol, filtered, concentrated to 50 ml. and cooled yielding 7.3 g. (92.5%) of pale yellow crystals, m.p. 114-117°. Ir, nmr, and ms support the structure.

Anal. Calcd. for $C_{21}H_{20}N_2O_4S$: C, 63.62; H, 5.08; N, 7.06; S, 8.09. Found: C, 63.56; H, 4.90; N, 7.15; S, 8.13.

Ethyl 4-Oxo-4*H*-dibenzo[*b,f*]pyrimido[1,2-*d*][1,4]thiazepine-3-carboxylate (**22**).

A solution of 4.0 g. (0.01 mole of **21** in 25 ml. of 1,2,4-trichlorobenzene was heated, under nitrogen, at reflux for 3 hours. After filtration the solution was diluted with pentane giving 3.33 g. (95%) of tan crystals, m.p. 199.5-201°. Recrystallization from 200 ml. of methanol yielded 2.94 g. of nearly white crystals, m.p. 202-203.5°; ir (Nujol): 1745, 1705, 1675 (C=O), 1580, 1560, 1500 (C=C/C=N), 1305, 1265, 1140, 1100 (C-O/other), 775 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.38 (t, 3, CH_2CH_3), 4.40 (q, 2, CH_2CH_3), between 7.1 and 8.0 (m, 8, arom. H's), 8.8 (s, 1, CH=); ms: M^+ 350.

Ethyl *N*-[Dibenzo[*b,f*]thiazepin-11-yl]malonate (**23**).

To a soluton of 1.59 g. (0.012 mole) of monoethyl malonate in 20 ml. of

tetrahydrofuran, under nitrogen, was added with stirring 2.11 g. (0.013 mole) of 1,1'-carbonyldiimidazol. After stirring for 10 minutes a solution of 2.26 g. (0.01 mole) of 11-aminodibenzo[*b,f*][1,4]thiazepin (9) in 100 ml. of tetrahydrofuran was slowly added. The solution was stirred for 21 hours at room temperature, concentrated *in vacuo*, and shaken with water giving a gum which soon solidified, m.p. 145-148°. This was dissolved in ether, washed with 1° aqueous acetic acid, then with water and dried over sodium sulfate. Filtration and evaporation *in vacuo* gave 2.89 g. of nearly white solid which was recrystallized from 2-propanol yielding 2.15 g. (63%) of white crystals, m.p. 148-149.5°. Further recrystallization of a sample from ether gave an analytical sample, m.p. 151-152°. Ir, nmr, and ms support the structure.

Anal. Calcd. for $C_{18}H_{16}N_2O_3S$: C, 63.51; H, 4.74; N, 8.23; S, 9.42. Found: C, 63.50; H, 4.65; N, 8.04; S, 9.30.

3-Carboxy-4-oxo-4*H*-dibenzo[1,2-*d*][1,4]thiazepine-2-acetic Acid Diethyl Ester (**24**).

In another preparation of **23** as above except a 50% excess of monoethyl malonate and 1,1'-carbonyldiimidazol were used, besides **23** and starting material, a third component was found by tlc (silica gel 60% ethyl acetate in cyclohexane). Fractional crystallization from ether, 2-propanol, and methanol gave a 4% of white crystals, m.p. 139-140°. The structure, **24**, was deduced from ir, nmr, ms and analysis. Ir (Nujol): 1735, 1720, 1690 (C=O), 1585, 1565, 1515 (C=C/C=N), 1335, 1280, 1195, 1185, 1085, 1065 (C-O/C-N/other, 775, 770 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.25 and 1.37 (two t, 6, (two CH_2CH_3), 3.94 (s, 2, $CH_2C=$), 4.3 (two overlapping q, 4, two CH_2CH_3), between 7.1 and 8.0 (m, 8, arom. H's); ms: M^+ 436.

Treatment of **23** with monoethyl malonate and 1,1'-carbonyldiimidazole did not give **24** and the **23** was recovered.

2-Hydroxy-4*H*-dibenzo[*b,f*]pyrimido[1,2-*d*][1,4]thiazepin-4-one, Salt with 11-Aminodibenzo[*b,f*][1,4]thiazepine (**25**) and Free Acid (**26**).

A solution of 1.7 g. (0.005 mole) of **23** in 15 ml. of xylene, under nitrogen, was stirred under reflux for 1 hour, during which crystals separated. The hot solution was filtered giving 0.8 g. (61%) of yellow-tan crystals, m.p. 241.5-243.5° dec. Recrystallization from 2-methoxyethanol yielded 0.6 g. of pale yellow solid, m.p. 240-242.5° dec. This was found to be a salt, **25**, of the two compounds indicated in the heading; ir (Nujol): 3120, 2700 (NH/OH/$\overset{+}{N}$H), 1660, 1615, 1585, 1575, 1560, 1480 (C=N/C=C/NH def./C=O), 1470, 1393, 1330, 1300 (C-N/CH/other); 765 (arom.) cm^{-1}.

A sample of this salt was treated with very dilute aqueous sodium hydroxide and extracted with methylene chloride. Evaporation of the methylene chloride yielded 11-aminodibenzo[*b,f*][1,4]thiazepine, identical with an authentic sample (9). The aqueous solution was acidified with acetic acid giving a white precipitate, which was collected, washed with water, dried and recrystallized from 2-methoxyethanol, m.p. 262-264° dec.; ir (Nujol): 3140 (OH), 1670, 1640 (C=O/C=C/C=N), 1590, 1575, 1560, 1525 (C=N/C=C), 1300, 1260, 1240, (C-O/C-N), 840 (other), 765 (arom.) cm^{-1}; nmr (DMSO-d_6): δ 5.55 (exchangeable with deuterium oxide) (s, 1, OH), between 7.1 and 8.0 (m, 9, =C-H and arom. H's); ms: M^+ 294.

3,3-Dimethyl-2*H*-dibenzo[*b,f*]pyrimido[1,2-*d*][1,4]thiazepine-2,4-(3*H*)dione (**27**).

A mixture of 2.26 g. (0.01 mole) of 11-aminodibenzo[*b,f*][1,4]thiazepine (9) and 1.3 ml. of triethylamine in 50 ml. of tetrahydrofuran was cooled, under nitrogen, to −80° and 3.16 ml. (0.025 mole) of dimethylmalonyl dichloride was slowly added with stirring. After stirring at room temperature for 3 days, the solvent was evaporated *in vacuo* and the residue was dissolved in methylene chloride. The solution was well extracted with cold dilute hydrochloric acid, and the acid extract was basified with cold aqueous sodium hydroxide. The product was extracted with methylene chloride, washed with water, dried and evaporated. The residue was crystallized from dimethylsulfoxide yielding 0.24 g. (13%) of white needles, m.p. 261-262.5°; ir (Nujol): 1740, 1695 (C=O), 1585, 1570, 1550 (C=N/C=C), 1350, 1300, 1275, 1120 (C-N/other), 770, 735 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.61 and 1.72 (two s's, 6, two CH_3's), between 7.15 and 8.15 (m, 8, arom. H's); ms: M^+ 322.

2-(Dimethylamino)-2,3-dihydro-3,3-dimethyl-4*H*-dibenzo[*b,f*]pyrimido[1,2-*d*][1,4]triazepin-4-one (**28**).

An attempt was made to prepare the above **27** in dimethylformamide in place of tetrahydrofuran. The product was chromatographed on silica gel, eluting with 5% methanol in chloroform. The only compound isolated was a 15% yield of 28, crystallized from ethyl acetate, m.p. 145.5-147.5°. Undoubtedly the dimethylamino group came from the dimethylformamide; ir (Nujol): 2770 (N-alkyl), 1700, 1690 (C=O), 1625 (C=N), 1580 (C=C), 1340, 1315, 1225, 1155, 1125 (C-N/other), 775, 760 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.38 and 1.5 (2 s's, 6, $C(CH_3)_2$), 2.54 (s, 6, $N(CH_3)_2$), 4.47 (s, 1, CH=), between 7.0 and 7.93 (m, 8, arom. H's); ms: M^+ 351.

N,N-Dimethyl-*N'*-(*o*-nitrophenyl-*N'*-phenylethylenediamine Hydrochloride (**29**).

A mixture of 53.6 g. (0.25 mole) of 2-nitrodiphenylamine, 12.5 g. (0.35 mole) of a 56% dispersion of sodium hydride in mineral oil, and 1 l. of dimethylformamide was vigorously stirred for 1 hour. Then 200 ml. of a benzene solution containing 0.45 mole of dimethylaminoethyl chloride was slowly added. After stirring at room temperature for 2 hours and 1 hour at 60° the mixture was concentrated *in vacuo* (at < 1 mm.). The resulting syrup was taken up in methylene chloride and extracted with dilute hydrochloric acid. The aqueous solution was washed with methylene chloride and basified with sodium hydroxide. The free base was extracted with methylene chloride, washed with water and evaporated *in vacuo*. The residue was dissolved in ether and acidified with ethanolic hydrogen chloride, and the resulting hydrochloride was recrystallized from a mixture of methanol and 2-propanol yielding 51.5 g. (64%) of yellow prisms, m.p. 190.5-192°. Ir, uv, and nmr support the structure.

Anal. Calcd. for $C_{16}H_{20}ClN_3O_2$: C, 59.71; H, 6.26; Cl, 11.02; N, 13.07. Found: C, 59.52; H, 6.19; Cl, 11.12; N, 12.98.

N,N-Dimethyl-*N'*-(*o*-aminophenyl)-*N'*-phenylethylenediamine Monohydrochloride (**30**).

A solution of 64.6 g. (0.2 mole) of **29** in 800 ml. of ethanol was hydrogenated with 800 mg. of platinum oxide at room temperature and 3.5 kg./cm^2 for 2 hours. The product partly separated and was dissolved by adding 200 ml. of methanol and heating to boiling. The hot solution was filtered through Supercel and evaporated *in vacuo*. The residue was crystallized from a mixture of methanol and 2-propanol yielding 57.8 g. (99%) of nearly white crystals, m.p. 249-252°. Ir and nmr support the structure.

Anal. Calcd. for $C_{16}H_{22}ClN_3$: C, 65.85; H, 7.60; Cl, 12.15; N, 14.40. Found: C, 65.80; H, 7.60; Cl, 12.20; N, 14.28.

[*o*-[*N*-[2-(Dimethylamino)ethyl]aniline]phenyl]urea (**31**).

A solution of 24 g. (0.08 mole) of **30** in 250 ml. of acetic acid, under nitrogen, was cooled to 0° and 7.4 g. (0.092 mole) of potassium cyanate was added. After stirring at room temperature for 22 hours the mixture was poured onto ice and basified with ammonium hydroxide. The product was extracted with chloroform and the extract was washed with saturated sodium chloride, dried over sodium sulfate, and evaporated *in vacuo*. Trituration of the residue with ether gave 19.2 g. (81%) of dark colored platelets, m.p. 141-143°. This was used in the preparation of **32** below. A sample recrystallized from ethyl acetate had m.p. 148-150°. Ir, uv, and ms supported the structure.

Anal. Calcd. for $C_{17}H_{22}N_4O$: C, 68.43; H, 7.43; N, 18.78. Found: C, 68.50; H, 7.54; N, 18.40.

11-Amino-5-[2-(dimethylamino)ethyl]-5*H*-dibenzo[*b,e*][1,4]diazepine (**32**) (10).

A mixture of 19.2 g. (0.068 mole) of **31**, 300 ml. of toluene, and 32.0 ml. (0.35 mole) of phosphoryl chloride, under nitrogen, was heated at 116°

with stirring for 3.5 hours. After cooling the solvent was removed *in vacuo* and the residue was basified with cold dilute ammonium hydroxide. The product was extracted with chloroform, the extract was washed with water, and evaporated *in vacuo*. Trituration of the residue with methylene chloride yielded 13.5 g. (83.5%) of solid, m.p. 154-157°. A sample was recrystallized from methylene chloride giving white crystals, m.p. 158-159°, showing one spot on tlc (silica gel, 10% methanol in chloroform), ir (Nujol): 3280, 3100 (NH), 2780 (*N*-alkyl), 1660, 1615, 1590, 1570, 1495, 1480 (C=N/NH def./=C), 1310, 1290, 1255, 1165, 1095, 1045 (C-N/other), 770, 765, 750, 740 (arom./other) cm^{-1}; nmr (deuteriochloroform): δ 2.33 (s, 6, CH_3's), 2.57 and 3.8 (two t's, 4, two NCH_2's), 5.57 (broad s, 2, NH_2), between 6.65 and 7.45 (m, 8, arom. H's); ms: M^+ 280, reported (10) from acetone/ether/petroleum ether, m.p. 160-161° and 167-168°.

Diethyl[[[5-Dimethylamino)ethyl]-5*H*-dibenzo[*b,e*][1,4]diazepin-11-yl]-amino]methylene]malonate Hydrochloride (**33**).

A mixture of 2.8 g. (0.01 mole) of **32** and 2.42 ml. (0.012 mole) of diethyl ethoxymethylenemalonate, under nitrogen, was stirred on a steam bath for 2 hours. The crude free base was dissolved in 150 ml. of ether and acidified with ethanolic hydrogen chloride. The resulting hydrochloride was recrystallized from 2-propanol yielding 0.9 g. (18.5%) of yellow crystals, m.p. 209-211° dec. Ir and nmr support the structure.

Anal. Calcd. for $C_{25}H_{31}ClN_4O$: C, 61.66; H, 6.41; Cl, 7.28; N, 11.50. Found: C, 61.77; H, 6.63; Cl, 7.43; N, 11.15.

Ethyl 10-[2-(Dimethylamino)methyl]4,10-dihydro-4-oxo-dibenzo[*b,f*]pyrimido[1,2-*d*][1,4]diazepine-3-carboxylate Dihydrochloride, Ethanol Solvate (**34**).

Crude free base of **33** was prepared on one-half the scale described above. Tlc (silica gel, 5% methanol in chloroform) showed one spot. This was dissolved in 10 ml. of 1,2,4-trichlorobenzene and stirred, under nitrogen, at reflux for 4 hours. The solvent was removed *in vacuo* and the residue was dissolved in ether and extracted with dilute hydrochloric acid. The extract was washed with ether and basified with ammonium hydroxide. The free base was extracted with methylene chloride, washed with water, saturated sodium chloride solution, and dried over magnesium sulfate. Filtration and evaporation *in vacuo* yielded 1.64 g. of light brown amorphous free base of **34**. This was chromatographed on dry silica gel, eluting with 15% methanol in chloroform. The resulting amorphous free base was converted to the hydrochloride in ethanol yielding 0.79 g. of yellow solid, m.p. 174-177° dec. This was found by ir and nmr to be the dihydrochloride-ethanol solvate, ms: M^+ 404 agrees for the free base.

10-[2-(Dimethylamino)ethyl]-4,10-dihydro-4-dibenzo[*b,f*]pyrimido[1,2-*d*]-[1,4]diazepine-3-carboxylic Acid Hydrochloride Hydrate (**35**).

Crude amorphous free base of the ester **34** was prepared as above from 2.8 g. (0.01 mole) of **32**. This was dissolved in 50 ml. of methanol and 7.5 ml. of 5.32 *N* aqueous sodium hydroxide was added. After stirring, under nitrogen, at room temperature for 5 hours the solution was filtered, acidified with hydrochloric and evaporated *in vacuo*. The residue was boiled with ethanol and filtered. The solid, a mixture of product and sodium chloride was separated by repeated boiling with methanol and filtering from the less soluble sodium chloride. Finally the product was recrystallized from water giving 2.5 g. (60%) of yellow crystalline hydrochloride-monohydrate, m.p. 276-278° dec. Ir, nmr and ms support the structure.

3,3,10-Trimethyldibenzo[*b,f*]pyrimido[1,2-*d*][1,4]diazepine-2,4-(3*H*,10*H*)-dione (**36**).

A solution of 2.24 g. (0.01 mole) of 11-amino-5-methyl-5*H*-dibenzo[*b,e*]-[1,4]diazepine (11) and 1.3 ml. of triethylamine in 25 ml. of tetrahydrofuran, under nitrogen, was cooled to −80° and 3.14 ml. (0.025 mole) of dimethylmalonyl dichloride was added dropwise with stirring. After stirring at room temperature for 24 hours and at 8° for 6.5 hours, the solvent was evaporated *in vacuo*. The residue was taken up in methylene chloride and extracted with cold dilute hydrochloric acid. The extract was basified with sodium hydroxide and extracted with methylene chloride. This solution of the free base was chromatographed on silica gel eluting with 5% methanol in chloroform. After evaporation the product was crystallized from ethyl acetate yielding 0.64 g. (21%) of pale yellow prisms, m.p. 218-219.5°. Ir, nmr and ms support the structure.

Ethyl 4-(Dibenzo[*b,f*][1,4]thiazepin-11-yl)allophanate (**37**) and Ethyl Dibenzo-2,4-dioxo[*b,f*]-*s*-triazino[1,4]thiazepine-3(2*H*,4*H*)carboxylate (**38**).

A solution of 4.52 g. (0.02 mole) of 11-aminodibenzo[*b,f*][1,4]thiazepine (9) in 50 ml. of tetrahydrofuran and 30 ml. of dimethylformamide was cooled to −80° under nitrogen, and 5.8 ml. (0.05 mole) of carbethoxyisocyanate (12) was added slowly with stirring. The mixture was stirred at room temperature for 4.5 hours evaporated *in vacuo* and crystallized from ethyl acetate yielding 2.3 g. (34%) of white crystals, m.p. 201-202.5°. The structure was found to be the allophanate (**37**) by ir, nmr and analysis; ir (Nujol): 3240, 3150 (NH), 1790, 1700 (C=O), 1635 (C=N), 1585, 1525, 1495 (C=C/amide II), 1305, 1250, 1235, 1180, 1125, 1085 (C-O/C-N), 775, 755 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.33 (t, 3, CH_2CH_3), 4.32 (q, 2, CH_2CH_3), between 7.05 and 8.2 (m, 8, arom. H's).

Anal. Calcd. for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31; S, 9.39. Found: C, 59.36; H, 4.60; N, 12.31; S, 9.02.

In another run under essentially the same conditions except the reaction was stirred overnight at room temperature, a 22% yield of white crystals was obtained, m.p. 229-230°. This was found by ir, nmr, ms and analysis to have the structure **38**; ir (Nujol): 1795, 1770, 1745, 1700 (C=O), 1585, 1570, 1560 (C=C/C=N), 1440, 1380, 1350, 1230, 1080 (other), 770 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.43 (t, 3, CH_2CH_3), 4.57 (q, 2, CH_2CH_3), between 7.2 and 8.1 (m, 8, arom. H's); ms: M^+ 367.

Dibenzo[*b,f*]-*s*-triazino[1,4]thiazepine-2,4(3*H*)dione (**39**).

A solution of 1.28 g. (0.0035 mole) of **37** in 20 ml. of xylene, under nitrogen, was stirred under reflux for 2.5 hours. After cooling the resulting solid was collected, washed with ether and dried, yielding 0.35 g. (34.5%) of white crystals, m.p. 314-315.5° dec.

A run was made from 18.08 g. (0.08 mole) of 11-aminodibenzo[*b,f*][1,4]-thiazepine without isolating the intermediate **37** giving a 56% overall yield of **39**, m.p. 314.5-317° dec.; ir (Nujol): 3200, 3140, 3010 (NH/OH), 1750, 1680 (C=O), 1585, 1565, 1545 (C=C/C=N), 1390, 1275 (other), 790, 785, 765 (arom.) cm^{-1}; nmr (DMSO-d_6): only bands between δ 7.25 and 8.0 (arom. H's and NH); ms: M^+ 295.

3-Methyl-2*H*-dibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]thiazepine-2,4-(3*H*)dione (**40**).

A mixture of 2.95 g. (0.01 mole) of **39** and 0.5 g. (0.014 mole) of 57% sodium hydride in mineral oil in 75 ml. of dimethylformamide, under nitrogen, was stirred at 95° for 1 hour. After cooling to room temperature 0.75 ml. (0.012 mole) of methyl iodide was slowly added and the mixture was stirred at 95° for 4 hours and 16 hours at room temperature. After evaporation of the solvent *in vacuo*, the residue was dissolved in methylene chloride, washed with water and again evaporated. The product crystallized from acetone yielding 1.41 g. (46%) of white crystals, m.p. 266-268°. Ir, nmr, and ms support the structure.

3-[3-(Dimethylamino)propyl]-2*H*-dibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]thiazepine-2,4(3*H*)dione (**41**).

A mixture of 2.95 g. (0.01 mole) of **39** and 0.5 g. (0.014 mole) of 57% sodium hydride in mineral oil in 65 ml. of dimethylformamide under nitrogen, was stirred at 60° for 2 hours. After cooling to room temperature 0.018 mole of 3-(dimethylamino)propyl chloride in benzene was slowly added and the mixture was stirred at 60° for 2 hours and overnight at room temperature. After evaporation of the solvent *in vacuo* the residue was dissolved in methylene chloride and extracted with cold dilute hydrochloric acid. The extract was washed with methylene chloride, basified with sodium hydroxide and extracted with methylene chloride. The methylene chloride solution was washed with water, evaporated *in vacuo* and crystallized from acetone-hexane yielding 0.5 g.

(13%) of white needles, m.p. 184-187°. Ir, nmr and ms support the structure.

Ethyl 4,10-Dihydro-10-methyl-2,4-dioxodibenze[*b,f*]-*s*-triazino[1,2-*d*][1,4]-diazepine-3(3*H*)carboxylate (**42**).

A solution of 4.47 g. (0.02 mole) of 11-amino-5-methyl-5*H*-dibenze-[*b,e*][1,4]diazepine (11) in 50 ml. of tetrahydrofuran, under nitrogen, was cooled to −80° and 5.8 ml. (0.05 mole) of carbethoxyisocyanate (12) was slowly added with stirring. The mixture was stirred at room temperature for 18 hours, evaporated *in vacuo*, and crystallized from ethyl acetate-hexane yielding 2.85 g. (39%) of nearly white solid, m.p. 230-232.5°. Ir, nmr and ms support the structure.

10-Methyldibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]diazepine-2,4-(3*H*,10*H*)dione (**43**).

To a mixture of 8.0 g. (0.022 mole) of **42** and 200 ml. of ethanol, under nitrogen, was slowly added, with stirring, 1.2 ml. (0.024 mole) of hydrazine hydrate. The mixture was stirred under reflux for 5.5 hours, concentrated to 100 ml. and cooled, yielding 5.55 g. (86%) of white prisms, m.p. 289-292°, ir (Nujol): 3120, 3000 (NH), 1745, 1680 (C=O), 1595, 1570, 1545, 1500 (C=C/C=N), 1390, 1280, 1245 (C-N/other), 795, 785, 775 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 3.37 (s, 3, NCH_3), between 7.0 and 8.1 (m, 9, arom. H's and NH); ms: M^+ 292.

3,10-Dimethyldibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]diazepine-2,4-(3*H*,10*H*)dione (**44**).

A mixture of 2.05 g. (0.007 mole) of **43**, 0.4 g. (0.0092 mole) of 56% sodium hydride in mineral oil, and 50 ml. of tetrahydrofuran, under nitrogen, was stirred at 95° for 45 minutes after cooling to room temperature. 0.75 ml. (0.015 mole) of methyl iodide was slowly added and the solution was stirred at 95° for 3 hours. The solvent was evaporated *in vacuo*, the residue was dissolved in methylene chloride, and washed with water. Evaporation of the methylene chloride *in vacuo* and crystallization from acetone-hexane yielded 1.0 g. (49%) of yellow crystals, m.p. 236-238°. Ir, nmr and ms support the structure.

3-[3-(Dimethylamino)propyl]-10-methyldibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]-diazepine-2,4-(3*H*,10*H*)dione (**45**).

A mixture of 2.92 g. (0.01 mole) of **43**, 0.5 g. (0.014 mole) of 56% sodium hydride in mineral oil, and 40 ml. of dimethylformamide, under nitrogen, was stirred at room temperature for 2 hours. Then 0.018 moles of a benzene solution of 3-(dimethylamino)propyl chloride was slowly added, and the mixture was stirred for 2 hours at room temperature and 2 hours at 60°. After removal of the solvent *in vacuo*, the residue was dissolved in methylene chloride and the product was extracted with dilute hydrochloric acid. The extract was basified with dilute sodium hydroxide, the free base was extracted with methylene chloride, and washed with water. Evaporation *in vacuo* and crystallization from 2-propanol yielded 2.7 g. (73%) of light yellow needles, m.p. 211.5-213°. Ir, nmr and ms support the structure.

Ethyl 10[2-Dimethylamino)ethyl]-2,10-dihydro-2,4-dioxodibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]diazepine-3-(4*H*)carboxylate (**46**), and Ethyl 4-[5-[2-Dimethylamino)ethyl]-5*H*-dibenzo[*b,e*][1,4]diazepin-11-yl]allophanate (**47**).

A solution of 5.62 g. (0.02 mole) of **32** in 50 ml. of tetrahydrofuran was cooled to 0°, under nitrogen, and 5.8 ml. (0.05 mole) of carbethoxyisocyanate (12) was slowly added with stirring. After stirring at room temperature for 18 hours, the solvent was removed *in vacuo* and the residue was chromatographed on silica gel, eluting with 2° methanol in chloroform. The major fraction was evaporated and crystallized from ether-methylene chloride giving 2.95 g. (71%) of yellow needles, m.p. 175.5-176°. The ir and the nmr were identical with **46** previously reported (3).

The second major fraction from the column was evaporated *in vacuo* and crystallized from ether-methylene chloride yielding 0.54 g. (7%) of yellow crystals, m.p. 131-134.5°. This was found by ir, nmr, ms and analysis to have the allophanate structure **47**; ir (Nujol): 2900 (broad) (NH), 1790, 1710 (C=O), 1625, 1590, 1545, 1510 (C=N/C=C/amide II), 1315, 1295, 1260, 1245, 1175, 1125, 1110, 1075 (C-O/C-N/other), 785, 775, 750 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 1.33 (t, 3, CH_2CH_3), 2.25 (s, 6, two CH_3's), 2.54 (t, 2, NCH_2), 3.84 (t, 2, NCH_2), 4.26 (q, 2, CH_2CH_3), between 6.88 and 7.14 (m, 9, arom. H's and NH); ms: no M^+ found, m/e 306 (M^+ - $H_2NCOOEt$), 294 (M^+ - CO_2Et) + CO), 280 (M^+ -O=C=NCOOEt), 222 (M^+ - O=C=NCOOEt) + $\cdot CH_2N(CH_3)_2$), 58 ($CH_2=\overset{+}{N}(CH_3)_2$).

Anal. Calcd. for $C_{21}H_{25}N_5O_3$: C, 63.78; H, 6.37; N, 17.71. Found: C, 63.63; H, 6.48; N, 17.73.

10-[2-(Dimethylamino)ethyl]-3-methyldibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]diazepine-2,4-(3*H*,10*H*)dione (**48**).

A mixture of 2.23 g. (0.006 mole) of 10-[2-(Dimethylamino)ethyl]dibenzo[*b,f*]-*s*-triazino[1,2-*d*][1,4]diazepine-2,4-(3*H*,10*H*)dione (3), and 0.375 g. (0.0087 mole) of 56% sodium hydride in mineral oil and 60 ml. of dimethylformamide, under nitrogen, was stirred at 90° for 2 hours. After cooling to room temperature 0.37 ml. (0.006 mole) of methyl iodide was added and the mixture was stirred at 90° for 5 hours. The solvent was removed *in vacuo* and the residue was dissolved in chloroform, washed with water and dried over sodium sulfate. The solution was concentrated, filtered, and chromatographed on silica gel. Elution with 2% methanol in chloroform yielded 0.49 g. (23%) of white crystals, m.p. 198-199.5°. Ir, nmr and ms support the structure.

2-(Morphanthridine)hydrazone of Ethyl Pyruvate (**49**).

To a solution of 1.12 g. (0.005 mole) of 6-hydrazinomorphanthridine (7) in 50 ml. of tetrahydrofuran, under nitrogen, was added 0.56 g. (0.005 mole) of ethyl pyruvate, the solution was stirred at room temperature for 20 hours, and evaporated *in vacuo*. The residue was dissolved in methylene chloride, washed with water and dried over sodium sulfate. Evaporation *in vacuo* and crystallization from ethyl acetate-hexane yielded 0.73 g. (44%) of yellow-solid, m.p. 141-145°. Ir, uv, and nmr support the structure.

Anal. Calcd. for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 70.77; H, 5.89; N, 12.87.

2-Methyl-9*H*-dibenzo[*c,f*]-*as*-triazino[4,3-*d*]azepin-1-one (**50**).

A solution of 0.8 g. (0.0029 mole) of unrecrystallized **49** in 5 ml. of acetic acid, under nitrogen, was refluxed for 2 hours, cooled, and neutralized with ice and aqueous sodium bicarbonate. The product was extracted with methylene chloride washed with water and dried over sodium sulfate. The solution was evaporated, chromatographed on silica gel, eluting with 5% methanol in chloroform, and crystallized from ethyl acetate-hexane giving 0.55 g. (69%) of pale yellow solid, m.p. 203-205° dec.; ir (Nujol): 1690 (C=O), 1605, 1585, 1555, 1500 (C=N/C=C), 775, 770 (arom.) cm^{-1}; nmr (deuteriochloroform): δ 2.61 (s, 3, CH_3), AB centered at 3.58 and 4.0 (2, J = 14 Hz, Ph_2CH_2), between 7.05 and 8.1 (m, 8, arom H's); uv max (ethanol): 220 mμ (ε 22,950), 245 (7,050), 308 (9,650).

2-Methyl-9*H*-dibenzo[*c,f*]-*as*-triazino[4,3-*d*][1,4]diazepin-1-one Ethyl Acetate and Methylene Chloride Solvate (**51**).

Free base was liberated from 5.2 g. (0.02 mole) of 11-hydrazino-5*H*-dibenzo[*b,e*][1,4]diazepine hydrochloride (13) with dilute sodium hydroxide and extracted with methylene chloride. After washing with water and drying over sodium sulfate, the solution was evaporated. The residue was dissolved in 100 ml. of tetrahydrofuran and treated with 2.32 g. (0.02 mole) of ethyl pyruvate under nitrogen. After standing at room temperature for 20 hours the mixture was evaporated *in vacuo*, dissolved in methylene chloride, washed with water and dried over sodium sulfate. Evaporation *in vacuo* gave the intermediate hydrazone as an oil, the structure of which was confirmed by nmr. This was dissolved in 50 ml. of acetic acid and refluxed for 1 hour. Most of the acetic acid was removed *in vacuo* and the residue dissolved in methylene chloride, washed with aqueous sodium bicarbonate, then with water, and dried over sodium sulfate. Evaporation *in vacuo* and crystallization from ethyl acetate gave 1.07 g. of yellow solid, m.p. 241-244° dec. An additional amount was ob-

tained from the filtrate. The total yield was 3.3 g. (60%). Ir, uv, and nmr support the structure but show the presence of solvents even after prolonged drying *in vacuo*.

2-Azido-α-phenyl-*o*-acetotoluidide (**52**).

A small sample of 2-benzylchloroacetanilide (14) in 40 ml. of acetonitrile was mixed with an excess of sodium azide in 10 ml. of water and stirred under reflux for 12 hours. After removal of the solvent *in vacuo*, the residue was mixed with water and extracted with ether. After evaporation of the ether the product was chromatographed on silica gel, eluting with 10% ethyl acetate in hexane. There was thus obtained the azide, **52**, as yellow platlets, m.p. 121°. Ir, nmr and ms support the structure.

Anal. Calcd. for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.62; H, 5.10; N, 20.93.

2-Amino-α-phenyl-*o*-acetotoluidide (**53**).

A solution of 1.5 g. (0.006 mole) of **52** in 60 ml. of ethanol was hydrogenated at 3.5 kg./cm² and room temperature with 0.3 g. of platinum oxide for 1.5 hours. Filtration, evaporation and crystallization from ether yielded 1.1 g. (82%) of white crystals, m.p. 112-113°. Ir, nmr, and ms support the structure.

The same compound was prepared by heating 0.51 g. (0.002 mole) of 2-benzylchloroacetanilide (14) with 40 ml. of methanolic ammonium at 100°, under pressure, for 3 hours. Evaporation and recrystallization from ether yielded 0.21 g. (44%) of white crystals, m.p. 111-112° having an ir identical with the above.

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.62; H, 6.93; N, 11.73.

2-Acetamido-α-phenyl-*o*-acetotoluide (**54**).

A solution of 0.444 g. (0.002 mole) of **53**, 0.31 ml. (0.003 mole) of acetic anhydride, under nitrogen, was cooled to 0° and a solution of 0.12 g. of 85% potassium hydroxide in 3 ml. of methanol was slowly added with stirring. After stirring at room temperature for 16 hours and evaporating *in vacuo* the residue was mixed with ice-water and extracted with methylene chloride. The extract was washed with water, dried over sodium sulfate, evaporated, and crystallized from ethyl acetate, yielding 0.24 g. (43%) of white prisms, m.p. 164-166°. Ir and nmr support the structure.

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.52; H, 6.41; N, 9.91.

N-(Morphanthridin-6-yl)-*N'*-carbethoxymethylurea (**55**).

A solution of 4.16 g. (0.02 mole) of 6-aminomorphanthridine (3) and 10 ml. of ethyl isocyanotoacetate in 75 ml. of tetrahydrofuran was kept at room temperature overnight, filtered and evaporated *in vacuo*. The residue was crystallized from 2-propanol yielding 4.77 g. (71%) of white crystals, m.p. 169-172°. Ir, nmr and mass spec. support the structure.

Anal. Calcd. for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 12.45. Found: C, 67.42; H, 5.75; N, 12.61.

N-[(11*H*-dibenz[*b,e*]azepin-6-yl)methyl]phthalimide (**56**).

A mixture of 14.5 g. (0.06 mole) of 6-(Chloromethyl)morphanthridine (14) and 11.12 g. (1.1 moles) of potassium phthalimide in 160 ml. of dimethylformamide was stirred at 80°, under nitrogen, for 4 hours. Concentration and cooling gave a precipitate which was recrystallized from dimethylsulfoxide yielding 10.4 g. (50%) of white crystals, m.p. 205.5-207.5°. A sample for analysis was recrystallized from chloroform yielding a chloroform solvate which still contained 2.12% (0.064 mole) of chloroform (by melt solvate) after drying overnight at 100° under high vacuum. Ir, nmr, and ms support the structure.

Anal. Calcd. for $C_{23}H_{16}N_2O_2 \cdot 0.064\ CHCl_3$: C, 76.94; H, 4.50; N, 7.78. Found: C, 77.12; H, 4.46; N, 7.85.

Diethyl (11*H*-Dibenz[*b,e*]azepin-6-yl-methyl)malonate (**57**).

To a solution of 3.8 ml. (0.025 mole) of diethyl malonate in 10 ml. of dimethyl formamide, under nitrogen, was added with stirring 1.01 g. (0.025 mole) of 57% sodium hydride in mineral oil. Then a solution of 3.4 g. (0.014 mole) of 6-chloromethylmorphanthridine (14) in 40 ml. of dimethylformamide was slowly added. After two days at room temperature the mixture was concentrated *in vacuo*, neutralized with dilute acetic acid, and extracted with ether. The extract was washed with water, dried over sodium sulfate, filtered and concentrated. Addition of pentane yielded 3.6 g. (70%) of white crystals, m.p. 84.5-86°. Ir and nmr support the structure.

Anal. Calcd. for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34; N, 3.83. Found: C, 71.99; H, 6.56; N, 3.75.

5,11-dihydro-6*H*-dibenz[*b,e*]azepine-$\Delta^{6\alpha}$-acetonitrile (**58**).

To a solution of 3.4 g. (0.014 mole) of 6-chloromethylmorphanthridine (14) in 50 ml. of dimethylsulfoxide was added 2.45 g. (0.05 mole) of sodium cyanide. After stirring at room temperature overnight, the mixture was poured into ice water giving tan solid which was recrystallized from 2-propanol yielding 2.43 g. (75%) of tan crystals, m.p. 151-153°. The nmr indicates the double bond is in the $\Delta^{6\alpha}$ position, ir (Nujol): 3270 (NH), 2190 (C≡N), 1615, 1585, 1565, 1490 (C=C), 770, 755, 725 (arom.) cm⁻¹; nmr (deuteriochloroform): δ 3.84 (s, 2, Ph_2CH_2), 2.20 (s, 1, CH=), between 6.8 and 7.53 (m, 8, arom. H's), 7.69 (broad s, 1, NH): ms: M^+ 232.

Morphanthridine 5-Oxide (**59**).

A solution of 1.94 g. (0.01 mole) of morphanthridine (*caution*: skin irritant) in 10 ml. of chloroform was slowly added with stirring to a solution of 2.59 g. (0.015 mole) of *m*-chloroperbenzoic acid in 20 ml. of ether at 0°. After stirring overnight at room temperature the mixture was poured into 10% hydrochloric acid in ice. The aqueous layer was washed with ether and basified with cold 10% sodium hydroxide. The product was extracted with ether, dried over sodium sulfate, filtered, and evaporated *in vacuo*. The residue was chromatographed on silica gel, eluting with 10% ethyl acetate in hexane. The product was crystallized from ethyl acetate-hexane yielding 0.5 g. (24%) of white needles, m.p. 125-126.5°; ir (Nujol): 1690 (C=O or C=N), 1595, 1580, 1495, 1470 (C=C) (C=N), 1330, 1265 (C-N/N-O/other); 765, 755, 715 (arom.) cm⁻¹; nmr (deuteriochloroform): δ 3.89 (s, 2, Ph_2CH_2), between 7.0 and 8.0 (m, 8, arom. H's); ms: M^+ 209. Comparison with an authentic sample shows this is not the isomeric 5,7-dihydro-6-(5*H*)morphanthridinone.

Anal. Calcd. for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.47; H, 4.99; N, 6.69.

N,N-Dimethyl-*N'*-(*o*-nitrophenyl)-*N'*-phenyl-1,3-propanediamine Hydrochloride (**60**).

This was prepared as described for **29** from 6.4 g. (0.03 mole) of 2-nitrodiphenylamine, 1.5 g. of 56% sodium hydride in mineral oil, and 0.054 mole of 3-(dimethylamino)propyl chloride in dimethyl formamide. The free base was converted to the hydrochloride and crystallized from 2-propanol yielding 4.1 g. (41%) of crystals, m.p. 152-155°. Ir supports the structure.

Anal. Calcd. for $C_{17}H_{22}ClN_3O_2$: C, 60.80; H, 6.60; N, 12.51. Found: C, 60.52; H, 6.55; N, 12.60.

N-(3-Dimethylaminopropyl)-*N*-phenyl-*o*-phenylenediamine Dihydrochloride (**61**).

The hydrochloride (**60**) was converted to the free base with sodium hydroxide, extracted with ether, washed with water and dried over sodium sulfate. Filtration and evaporation gave free base as a dark syrup. A solution of 25 g. (0.03 mole) of this crude free base in 200 ml. of ethanol was hydrogenated at room temperature and 3.5 mg./cm² with 1.2 g. of platinum oxide. Filtration and evaporation *in vacuo* gave an oil which was converted to the dihydrochloride in methylene chloride with an excess of ethanolic hydrogen chloride. Recrystallization from methanol-2-propanol yielded 21.9 g. (67%) of crystals, m.p. 235-237°. Ir, nmr and ms support the structure.

Anal. Calcd. for $C_{17}H_{25}Cl_2N_3$: C, 59.65; H, 7.36; Cl, 20.72; N, 12.28. Found: C, 59.48; H, 7.51; Cl, 20.82; N, 12.26.

[*o*-[*N*-[3-(Dimethylamino)propyl]anilino]phenyl]urea (**62**).

This compound was prepared by the procedure described for **31** from 6.84 g. (0.02 mole) of **61** and 1.78 g. (0.022 mole) of potassium cyanate in 60 ml. of acetic acid. The crude free base was crystallized from methylene chloride-ether yielding 2.5 g. (36.4%) of white prisms, m.p. 167.5-169.5°. Ir, nmr and ms support the structure.

Anal. Calcd. for $C_{18}H_{24}N_4O$: C, 69.20; H, 7.74; N, 17.94. Found: C, 69.42; H, 7.93; N, 17.95.

Hydrochloride **63**.

A sample of **62** in methanolic hydrogen chloride was diluted with 2-propanol. The hydrochloride separated as white needles, m.p. 221-222°. Ir and nmr support the structure.

Anal. Calcd. for $C_{18}H_{25}ClN_4O$: C, 61.97; H, 7.22; Cl, 10.16; N, 16.06. Found: C, 62.31; H, 7.40; Cl, 9.87; N, 15.91.

9-[2-(Dimethylamino)ethyl]-*N,N*-dimethylthioxanthrene-9-carboxamide (**64**).

A mixture of 4.04 g. (0.015 mole) of *N,N*-dimethylthioxanthrene-9-carboamide (16) and 0.64 g. (0.0165 mole) of sodium amide in 35 ml. of toluene, under nitrogen, was stirred under reflux for 3 hours, cooled and a solution of 2.16 g. (0.015 mole) of 2-(dimethylamino)ethyl chloride in toluene was added. After refluxing for 2 hours and standing at room temperature overnight, water was added and the layers were separated. The toluene layer was extracted with dilute hydrochloric acid and the aqueous solution was basified with sodium hydroxide. The free base was extracted with methylene chloride, washed with water and dried over sodium sulfate. Evaporation *in vacuo*, and crystallization from ethyl acetate-hexane gave 2.1 g. (61%) of white crystals, m.p. 128-131°. Ir, uv, nmr and ms support the structure.

Anal. Calcd. for $C_{20}H_{24}N_2OS$: C, 70.55; H, 7.10; N, 8.23; S, 9.42. Found: C, 70.35; H, 7.13; N, 8.34; S, 9.67.

[3-(10,11-Dihydro-5*H*-dibenz[*b,f*]azepin-5-yl)propyl]trimethylammonium Iodide. (Imipramine Methiodide) (**65**).

A solution of 2.8 g. (0.01 mole) of 5-[3-(dimethylamino)propyl]-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (imipramine free base, Ib) and 14.2 g. (0.1 mole) of methyl iodide in 20 ml. of 2-butanone was stirred at room temperature for 1 hour. The resulting solid was collected and recrystallized from acetone yielding 3.25 g. (77%) of white prisms, m.p. 235-237°. Ir, nmr and ms support the structure.

Anal. Calcd. for $C_{20}H_{27}IN_2$: C, 56.87; H, 6.44; I, 30.05; N, 6.63. Found: C, 56.94; H, 6.60; I, 29.88; N, 6.43.

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