mmol) of **20** in 300 mL of H_2O and 60 mL of 10% aqueous NaOH was added 216 mg (5.6 mmol) of $NaBH_4$. The resulting slurry was stirred for 18 h as a light yellow solution gradually developed. The product was precipitated by the slow addition of 10% aqueous HCl to pH 2.0. The crystals were collected, washed with H_2O, and dried to give 1.8 g (88%) of product: mp 179–181 °C (acetone/*i*-PrOH); IR (KBr) 2.90 (broad NH and OH), 5.76 and 5.87 (CO), 6.68, 7.16, 7.46, 9.01, 9.16, 11.50 μm; mass spectrum, *m/e* 363. Anal. ($C_{16}H_{11}Cl_2N_3O_3 \cdot 0.25H_2O$) C, H, N.

Acknowledgment. We are grateful for the technical assistance of R. H. Allen, E. J. Feeney, J. Homiski, J. L. Kivlin, G. Mankewicz, and R. W. Sumner. R. W. Sumner also helped to prepare the manuscript.

Registry No. **1**, 83437-12-1; **5a**, 50274-85-6; **5b**·HCl, 83437-13-2; **5c**·HCl, 83437-14-3; **6a**, 7073-36-1; **8a**, 50274-64-1; **10c**, 83437-15-4; **11a**, 53334-38-6; **12c**, 83437-16-5; **13a**, 53266-65-2; **14a**, 83437-29-0; **14c**, 40913-56-2; **15**, 38571-25-4; **16**, 38571-18-5; **17**, 83437-17-6; **18**, 38571-18-5; **19**, 38571-27-6; **20**, 38571-19-6; **21**, 83437-18-7; **22**, 83437-19-8; **23**, 38571-37-8; **24**, 57715-86-3; **25**, 38571-26-5; **26**, 38571-28-7; **27**, 38571-35-6; **28**, 38571-34-5; **29**, 38571-36-7; **30**, 38571-38-9; **31**, 38560-82-6; **32**, 83437-20-1; **33**, 83437-21-2; **34**, 83437-22-3; **35**, 38561-06-7; **36**, 38561-08-9; **37**, 38561-07-8; **38**, 83437-23-4; **39**, 83437-24-5; **40**, 83437-25-6; **41**, 83437-26-7; **42**, 83437-27-8; **43**, 83437-28-9; **44**, 38560-76-8; *m*-acetotoluidide, 537-92-8; benzoyl chloride, 98-88-4; 4-amino-2-methylbenzophenone, 30086-89-6; chlorobenzene, 108-90-7; cyanoacetylurethane, 6629-04-5; malonyldiurethane, 49754-15-6.

2-Benzazepines. 2.[1,2] Thiazolo[5,4-*d*][2]benzazepines

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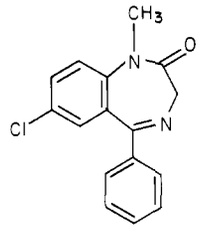
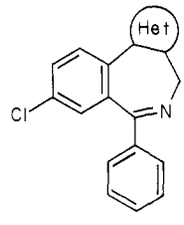
As part of a program in the area of annelated 2-benzazepines, several thiazolo[5,4-*d*][2]benzazepines were prepared. Treatment of the bromo ketones **7–9** with various thio amides gave the thiazoles **10–15**, which when treated with methylamine gave the title compounds. The preliminary pharmacology of these compounds showed that they had central nervous system activity similar to the 1,4-benzodiazepines, such as diazepam. The thiazolo[5,4-*d*][2]benzazepines were also found to bind to the benzodiazepine–receptor complex, indicating that their pharmacological actions are probably related to the 1,4-benzodiazepines.

Although an extensive amount of work has been done in the area of 1,4-benzodiazepines, such as diazepam (**1**), especially in regards to their use as anxiolytic agents,[3] very little information exists on the chemistry and/or pharmacology of the corresponding 1-carbon isoteres, the 2-benzazepines, especially 4,5-heterocyclic-fused compounds, **2**.[4]



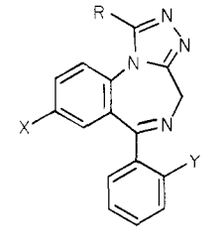
1 (diazepam)



2 (4,5-fused 2-benzazepine)

A further impetus toward preparing compounds of general structure **2** was provided by the triazolo-1,4-benzodiazepines, **3**, discovered by Upjohn.[5] These triazolo-1,4-benzodiazepines, depending on the substituents, have pharmacological profiles ranging from anxiolytics to hypnotics.

One generalization about the activity of the 1,4-benzodiazepines is that along with anxiolytic properties, there is always various degrees of sedation, muscle relaxation, and anticonvulsant, ataxia, and ethanol potentiating effects. Therefore, a program in the area of 4,5-heterocyclo-2-benzazepines was undertaken in an attempt to prepare compounds that might show anxiolytic activity with possibly a different profile than the 1,4-benzodiazepines.



3

The following is an account of the synthesis and pharmacological activity of novel thiazolo[5,4-*d*][2]benzazepines.

Chemistry. The starting materials for the preparation of thiazolo[5,4-*d*][2]benzazepines were the acetylenic compounds **1–3** described by Trybulski et al.[2] Hydration of **1–3** with formic acid/water in the presence of mercuric sulfate gave the ketones **4–6**. Bromination of **4–6** with cupric bromide yielded the bromo ketones **7–9**, which condensed readily with thiourea or thioacetamide to give the thiazoles **10–15**. Removal of the phthaloyl group by treatment of **10–15** with methylamine gave the thiazolo-[5,4-*d*][2]benzazepines **16–21**; see Scheme I. The melting points and yields for compounds **4–21** are listed in Tables I–III.

A less efficient synthesis of compound **17** started with the alcohol **22** and is outlined in Scheme II. Oxidation of **22** with pyridinium chlorochromate gave the aldehyde **23**, which was further oxidized by the method of Corey et al.[6] and gave the methyl ester **24**. Condensation of **24** with the anion of acetonitrile gave the keto nitrile **25**. Treatment of **25** with cupric bromide gave the bromo ketone **26**, which, without purification, was condensed with thiourea to give the thiazole **27**. Treatment of **27** with acetic an-

(1) Dedicated to the memory of Dr. Willy Leimgruber who died July 8, 1981.
(2) Paper 1: Trybulski, E. J.; Reeder, E.; Blount, J. F.; Walser, A.; Fryer, R. I. *J. Org. Chem.* **1982**, *47*, 2441.
(3) Sternbach, L. H. "The Benzodiazepines"; Garattini, S.; Mussini, E.; Randall, L. O., Eds.; Raven Press: New York, 1973; pp 1–26. Gschwend, H. W. "Anxiolytics"; Fielding, S.; Lal, H., Eds; Futura Publishing Co.: Mt. Kisco, NY, 1979; pp 1–40.
(4) During the course of this work, a patent appeared describing the synthesis of pyrazolo-2-benzazepines: Gschwend, H. U.S. Patent 3 947 585, 1976.
(5) Rudzik, A. D.; Hester, J. B.; Tang, A. H.; Straw, R. N.; Friis, W. In ref 3, pp 285–297.
(6) Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616.

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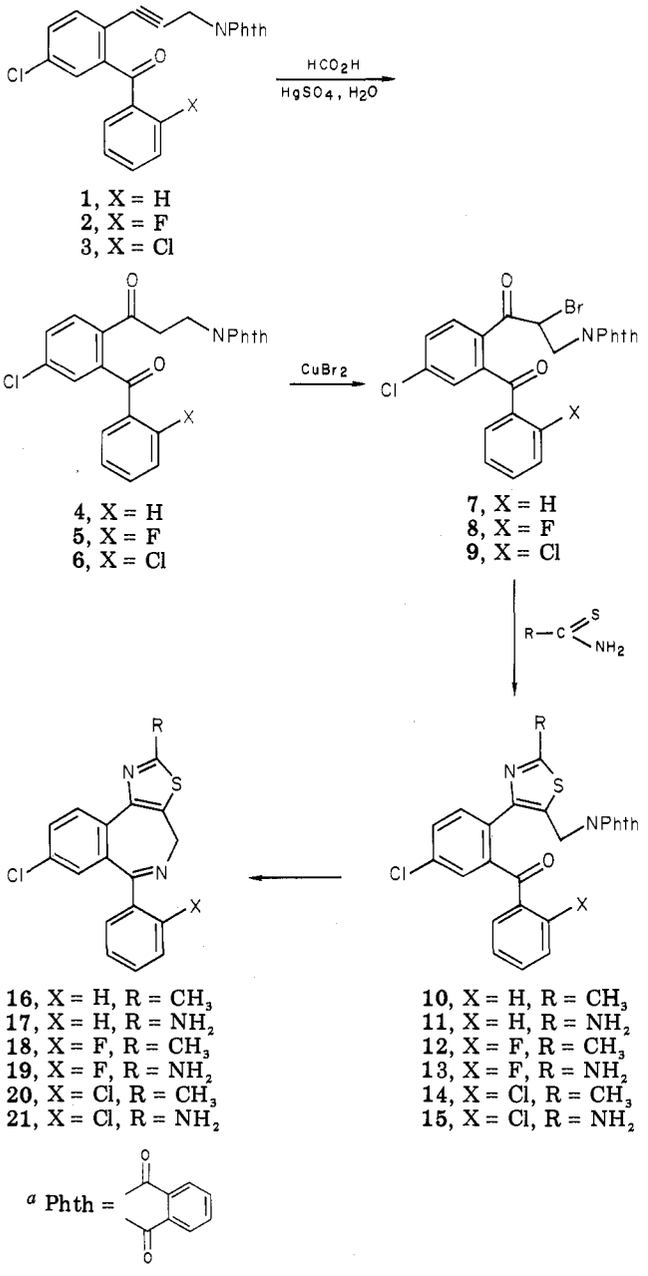
Scheme I[a]



1, X = H
2, X = F
3, X = Cl

4, X = H
5, X = F
6, X = Cl

7, X = H
8, X = F
9, X = Cl

16, X = H, R = CH_3
17, X = H, R = NH_2
18, X = F, R = CH_3
19, X = F, R = NH_2
20, X = Cl, R = CH_3
21, X = Cl, R = NH_2

10, X = H, R = CH_3
11, X = H, R = NH_2
12, X = F, R = CH_3
13, X = F, R = NH_2
14, X = Cl, R = CH_3
15, X = Cl, R = NH_2

[a] Phth =

Table I. Phthalimido Ketones 4-6 and the Corresponding Bromo Ketones 7-9

compd	formula[a]	mp, °C	yield, %
4	$C_{24}H_{16}ClNO_4$	156-157	65[b]
5	$C_{24}H_{15}ClFNO_4$	154-156	87
6	$C_{24}H_{15}Cl_2NO_4$	133-134	92
7	$C_{24}H_{15}BrClNO_4$	136-138	57
8	$C_{24}H_{14}BrClFNO_4$	125-128	58
9	$C_{24}H_{14}BrCl_2NO_4$	178-179	79

[a] C, H, N analyses were within ±0.4% of the theoretical values. [b] Reference 2.

Table II. Thiazolo Ketones 10-15

compd	formula[a]	mp, °C	yield, %
10	$C_{26}H_{17}ClN_2O_3S$	214-216	95
11	$C_{25}H_{16}ClN_3O_3S$	253-255	78
12	$C_{26}H_{16}ClFN_2O_3S$	228-230	99
13	$C_{25}H_{15}ClFN_3O_3S$	246-248	93
14	$C_{26}H_{16}Cl_2N_2O_3S$	238-240	98
15	$C_{25}H_{15}Cl_2N_3O_3S$[b]	238-240	100

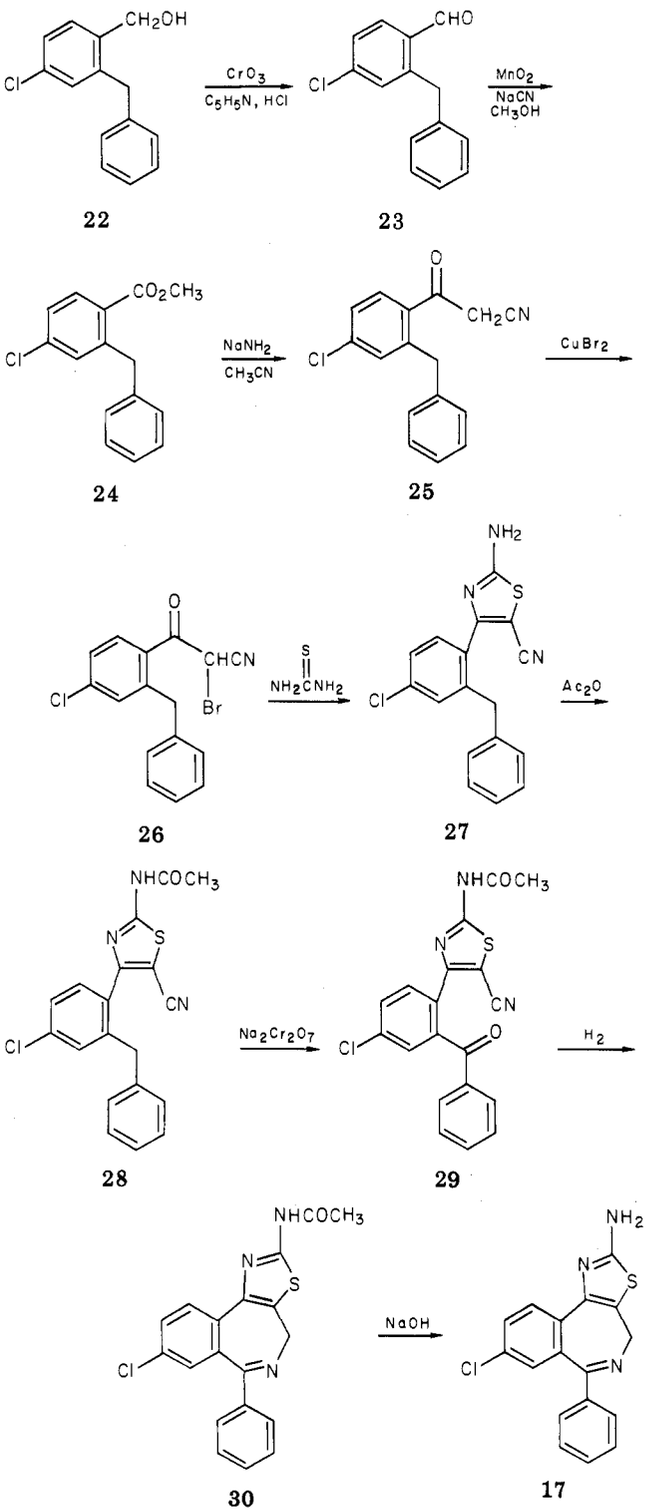
[a] See footnote a, Table I. [b] Product contained 0.3 mol of methylene chloride as determined by NMR.

Table III. Thiazolo[5,4-*d*][2]benzazepines 16-21

compd	formula[a]	mp, °C	yield, %
16	$C_{18}H_{13}ClN_2S$	128-130	65
17	$C_{17}H_{12}ClN_3S$	244-246	53
18	$C_{18}H_{12}ClFN_2S$	147-149	22
19	$C_{17}H_{11}ClFN_3S$	248-250	27
20	$C_{18}H_{12}Cl_2N_2S$	162-161	78
21	$C_{17}H_{11}Cl_2N_3S$	255-257	47

[a] See footnote a, Table I.

Scheme II



hydride gave **28**, which was oxidized to the ketone **29**. Hydrogenation of **29** with Raney nickel as catalyst gave

Table IV. Pharmacological Activity of Compounds 16-21

compd	antimetrazole:[a] ED_{50}, mg/kg po	[^{3}H]diazepam binding:[b] IC_{50}, nm
16	63 (43-92)	32
17	7.4 (4-11)	10.5
18	30 (21-43)	7.8
19	7.7 (5.5-10.4)	2.8
20	50 (31-140)	4.1
21	9.3 (2.3-33)	1.6
diazepam	1.0	5.0

[a] The test compound, dispersed in 5% acacia, was administered to three male CF-1 per dose level. One hour later, metrazole (70 mg/kg) was administered iv. The dose at which 50% of the animals are protected from convulsive seizures is expressed as the ED_{50}. [b] Interaction in vitro at benzodiazepine receptors was evaluated with [^{3}H]diazepam in the binding assay according to the procedure of Möhler, H.; Okada, T. *Life Sci.* 1977, *20*, 2101.

directly the cyclized 2-benzazepine **30**. Basic hydrolysis of **30** gave the amine **17**, identical with the product prepared by the method of Scheme I.

Pharmacology. The thiazole-2-benzazepines **16–21** were evaluated in both the [^{3}H]diazepam binding assay and in the antimetrazole test (prevention of metrazole-induced convulsions). These results are shown in Table IV, along with the comparative data for diazepam. The three amino compounds **17**, **19**, and **21** were all more active than the corresponding methyl compounds **16**, **18**, and **20** in the antimetrazole test. This trend of the amino compounds being more potent than the corresponding methyl compounds was also evident in the [^{3}H]diazepam binding assays. In general, the thiazolo-2-benzazepines were less active than other heterocyclic-fused 2-benzazepines.[7] The introduction of a 2′-halogen substituent did not markedly improve the antimetrazole activity (compare **16**, **18**, **20** and **17**, **19**, **21**). This is in contrast to the 1,4-benzodiazepines in which a rank order of activity for 2′-substituents is F > Cl > H. Compound **17** was evaluated in a few secondary screens and gave the following profile: foot shock, inactive; inclined screen, inactive; rotorod ED_{50} = 28 mg/kg; LD_{50} > 1000 mg/kg. The corresponding values for diazepam were: foot shock, 10 mg/kg; inclined screen, 25 mg/kg; rotorod ED_{50} = 3.2 mg/kg; LD_{50} > 1000 mg/kg. These data would indicate that compound **17** should have less muscle relaxation and ataxic properties than diazepam. In conclusion, 1,4-benzodiazepine-type activity has been demonstrated for thiazolo-2-benzazepines. The 2-methyl compounds **16**, **18**, and **20** were considered too weak in the antimetrazole test to be considered for further development, and the potential for mutagenicity with the 2-amino compounds **17**, **19**, **21** precluded their further development. The acetylated compound **30** had an antimetrazole value of ED_{50} = 15 mg/kg (11–20 mg/kg), which was weaker than the corresponding amine **17**. The amides of the other two amines **19** and **21** were not prepared.

Experimental Section

Melting points were determined in open capillary tubes and are corrected. Infrared spectra were determined on a Beckmann IR-9 or a Perkin-Elmer 621 grating spectrometer; mass spectra were determined on a CEC-21-100 instrument; and nuclear magnetic resonance spectra were performed on either a Varian A-60 or HA-100 spectrometer, with tetramethylsilane as an internal standard. Generally, only the main spectral peaks are reported, although all spectral data were consistent with the assigned structures. Merck silica gel 60, 70–230 mesh, was used for all column chromatography separations. Either anhydrous sodium sulfate or magnesium sulfate was used for drying of organic solutions.

2-[3-[4-Chloro-2-(2-fluorobenzoyl)phenyl]-3-oxopropyl]-1*H*-isoindole-1,3(2*H*)-dione (5). A stirred suspension of 1 g (0.01 mol) of mercuric sulfate in 55 mL of formic acid, 5 mL of H_2O, and 50 mL of CH_2Cl_2 was treated at room temperature over 5 min with 20.9 g (0.05 mol) of **2**. After stirring for 40 min, the mixture was poured into 250 mL of ice–water and extracted with CH_2Cl_2, and the extract was dried and evaporated in vacuo. Crystallization of the residue from 50 mL of 10% AcOEt in ether gave 19 g (87%) of light tan solid. Recrystallization of a sample from 2:1 CH_3OH/CH_2Cl_2 solution gave white crystals: mp 154–156 °C; IR ($CHCl_3$) 1776, 1718, 1687, 1675 cm^{-1}; NMR ($CDCl_3$) δ 3.29 (2 H, t, J = 16 Hz, CH_2), 3.96 (2 H, t, J = 12 Hz, CH_2), 6.9–7.95 (11 H, m, aromatic).

By the same procedure, compounds **4** and **6** were prepared from **1** and **3**, respectively.

2-[3-(2-Benzoyl-4-chlorophenyl)-2-bromo-3-oxopropyl]-1*H*-isoindole-1,3(2*H*)-dione (7). A stirred mixture of 36 g (0.086 mol) of **4**, 36 g (0.161 mol) of cupric bromide, 888 mL of THF, 48 mL of AcOEt, and 48 mL of $CHCl_3$ was refluxed for 30 min, cooled, diluted with about 800 mL of CH_2Cl_2, and filtered. The green filtrate was washed with H_2O, dried, and concentrated at reduced pressure to give a yellow gum, which crystallized from ether to give 24.2 g (57%) of off-white crystals. Recrystallization of a sample from a 2:1 mixture of EtOH and CH_2Cl_2 gave white crystals: mp 136–138 °C; UV max 219 nm (ϵ 58 100), 240 (sh, 22 000), 255/7 (16 600), 295 (sh, 5300); IR (KBr) 1775, 1718, 1708, 1685 cm^{-1}.

By the same procedure, compounds **8** and **9** were prepared from **5** and **6**, respectively.

2-[[4-(2-Benzoyl-4-chlorophenyl)-2-methyl-5-thiazolyl]-methyl]-1*H*-isoindole-1,3(2*H*)-dione (10). A mixture of 7.5 g (0.015 mol) of **7**, 2.25 g (0.03 mol) of thioacetamide, and 105 mL of 10% sulfur dioxide in DMF was heated on a steam bath under a drying tube for 1 h. The reddish-orange solution was poured over ice, and the resulting reddish-brown solid was collected by filtration, washed with H_2O, and air-dried to give 6.7 g (95%) of **10**. Recrystallization of a sample from $EtOH/CH_2Cl_2$ gave off-white needles: mp 214–216 °C; IR (KBr) 1771, 1711, 1671, 1615 cm^{-1}; NMR (Me_2SO-d_6) δ 2.26 (3 H, s, CH_3), 4.93 (2 H, s, CH_2), 7.20–7.88 (12 H, m, aromatics).

By the same procedure, compounds **12** and **14** were prepared from **8** and **9**, respectively.

2-[[2-Amino-4-(2-benzoyl-4-chlorophenyl)-5-thiazolyl]-methyl]-1*H*-isoindole-1,3(2*H*)-dione (11). A stirred solution of 10 g (0.02 mol) of **7** and 2 g (0.026 mol) of thiourea in 60 mL of EtOH, protected by a drying tube, was refluxed for 1 h. The yellow solution was poured over ice and diluted with H_2O. The pale yellow solid was collected by filtration, washed with H_2O, and air-dried on the funnel to give 7.4 g (78%) of product. Recrystallization of a sample from CH_3OH/CH_2Cl_2 gave pale yellow crystals: mp 253–255 °C; IR (KBr) 3425, 1775, 1713, 1658, 1620 cm^{-1}; NMR (Me_2SO-d_6) δ 4.68 (2 H, s, CH_2), 6.73 (2 H, s, NH_2), 7.05–7.87 (12 H, m, aromatics).

By the same procedure, compounds **13** and **15** were prepared from **8** and **9**, respectively.

8-Chloro-2-methyl-6-phenyl-4*H*-thiazolo[5,4-*d*][2]benzazepine (16). A mixture of 6.7 g (0.014 mol) of compound **10**, 56 mL of 40% aqueous CH_3NH_2, and 80 mL of EtOH was stirred at room temperature for 2 h. The dark solution was evaporated in vacuo, and the residue was partitioned between CH_2Cl_2 and H_2O. The organic phase was dried and concentrated in vacuo. The residue was stirred with boiling ether, cooled, and filtered. Evaporation of the filtrate gave a dark gum, which was filtered over silica gel with a solution of 2% AcOEt in CH_2Cl_2, followed by 5% AcOEt in CH_2Cl_2. Evaporation of the latter fractions gave 4.4 g of dark oil, which crystallized on standing. Recrystallization from ether/petroleum ether gave 3 g (65%) of tan crystals. A second recrystallization of a sample gave off-white prisms: mp 128–130 °C; IR ($CHCl_3$) 1610, 1701 cm^{-1}; NMR ($CDCl_3$) δ 2.72 (3 H, s, CH_3), 4.47 (2 H, s, CH_2), 7.30–8.07 (8 H, m, aromatic).

By the same procedure, compounds **18** and **20** were prepared from **12** and **14**, respectively.

8-Chloro-6-phenyl-4*H*-thiazolo[5,4-*d*][2]benzazepin-2-amine (17). A mixture of 6 g (0.0127 mol) of compound **11**, 120

(7) Unpublished results from these laboratories.

mL of 40% aqueous CH_3NH_2, and 180 mL of EtOH was stirred at room temperature for 1.5 h. Evaporation in vacuo gave a gum, which crystallized from a small amount of CH_3OH to give 2.2 g (53%) of tan crystals. Recrystallization of a sample from EtOH/CH_2Cl_2 gave pale yellow prisms: mp 244–246 °C dec; MS, m/e 325 (M^+), 297, 290, 266.

By the same procedure compounds **19** and **21** were prepared from **13** and **15**, respectively.

2-Benzyl-4-chlorobenzaldehyde (23). To a solution of 99.4 g (0.43 mol) of **22**[8] in 1 L of CH_2Cl_2 was added 276 g (1.28 mol) of pyridinium chlorochromate. After stirring for 1 h at room temperature, the mixture was diluted with 3 L of a 1:1 mixture of Et_2O and petroleum ether (bp 30–60 °C). The inorganic solids were removed by filtration, and the filtrate was concentrated under reduced pressure to give 90.5 g (91%) of **23** as an oil, which was used without further purification.

Methyl 2-Benzyl-4-chlorobenzoate (24). A solution of 5.51 g (0.11 mol) of NaCN in 550 mL of CH_3OH was added to 5.2 g (0.023 mol) of **23**. Following the addition of 40 g (0.45 mol) of MnO_2, the mixture was stirred at room temperature for 6 h. The inorganic salts were removed by filtration, and the filtrate was concentrated in vacuo. The residue was partitioned with CH_2Cl_2 and H_2O. The organic phase was separated, dried, and concentrated to give 5.2 g (87%) of **24** as an oil. The analytical sample was prepared by bulb distillation and obtained as a faint yellow oil: bp ~175 °C (0.3 mm); IR (neat) 1727 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3.75 (s, 3 H, CH_3), 4.33 (s, 2 H, CH_2), 7.05–7.90 (m, 8 H, aromatics). Anal. ($C_{15}H_{13}ClO_2$) C, H.

3-Oxo-3-(4-chloro-2-benzylphenyl)propanenitrile (25). A solution of $NaNH_2$ in NH_3 was prepared from 0.76 g (33.2 mmol) of Na and 40 mL of liquid NH_3. A solution of 1.36 g (33.2 mmol) of CH_3CN in 2 mL of Et_2O was then added, followed by a solution of 4.33 g (16.6 mmol) of **24** in 5 mL of Et_2O. After stirring for 1 h, the mixture was warmed on the steam bath to remove the NH_3. Ether was added at intervals in order to maintain a constant volume. After standing overnight, the reaction mixture was poured over ice and washed with AcOEt. The aqueous phase was acidified with 6 N HCl and extracted with AcOEt. The organics were dried and concentrated. The residue was filtered through silica gel with an ether–hexane mixture to give 3.45 g (77%) of **25**. An analytical sample was prepared by recrystallization from CH_2Cl_2/hexane and obtained as buff needles: mp 85–87 °C; IR (KBr) 2265 (CN), 1690 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3.76 (s, 2 H, CH_2CN), 4.23 (s, 2 H, CH_2), 7.00–7.58 (m, 8 H, aromatics). Anal. ($C_{16}H_{12}ClNO$) C, H, N.

2-Amino-4-(2-benzyl-4-chlorophenyl)-5-thiazolecarbonitrile (27). A mixture of 15 g (0.056 mol) of **25**, 22.5 g (0.101 mol) of cupric bromide, 8.4 g (0.056 mol) of 1,2-epoxy-3-phenoxypropane, 560 mL of THF, 30 mL of AcOEt, and 30 mL of $CHCl_3$ was refluxed with stirring for 5 h. The mixture was cooled, diluted with 750 mL of CH_2Cl_2, and filtered. The green filtrate was washed with water, dried, and evaporated in vacuo to give **26** as an oil. After **26** was dissolved in 150 mL of EtOH and 4.5 g (0.059 mol) of thiourea was added, the solution was protected by a drying tube and refluxed for 2 h. Evaporation of the solvent at reduced pressure gave an oil, which crystallized after washing successively with Et_2O and H_2O to give 5.3 g of tan crystals. Another 2.5 g of crystals was obtained by reworking the Et_2O wash to give a total yield of 7.8 g (43%). Recrystallization of a sample from EtOH (15 mL/g) gave off-white prisms: mp 210–212 °C; IR (KBr) 3370, 3285, 3120, 2225, 2210 cm^{-1}; UV max (EtOH) 215 nm (sh, ϵ 25 300), 247 (11 000), 303 (8300); NMR (Me_2SO-d_6) δ 4.08 (s, 2 H, CH_2), 6.90–7.40 (m, 8 H, aromatic), 8.18 (s, 2 H, NH_2); MS, m/e 324 (M^+). Anal. ($C_{17}H_{12}ClN_3S$) C, H, N.

***N*-[4-(2-Benzyl-4-chlorophenyl)-5-cyanothiazol-2-yl]acetamide (28).** A stirred suspension of 16.6 g (0.051 mol) of **27** in 85 mL of Ac_2O was heated under reflux for 45 min. After cooling, the solution was poured into 800 mL of ice–water with stirring. Stirring was continued for 45 min, and all lumps were crushed. The off-white solid was collected by filtration, washed with H_2O, and air-dried to give 18.7 g (100%) of **28**. Recrystallization of a sample from EtOH (10 mL/g) gave off-white prisms, which melted at 183–185 °C and again at 196–197 °C after resetting: IR (KBr) 3275, 2215, 1698, 1525 cm^{-1}; UV max (EtOH) 215 nm (sh, ϵ 24 100), 252 (19 800), 291 (9400); NMR (Me_2SO-d_6) δ 2.24 (s, 3 H, CH_3), 4.08 (s, 2 H, CH_2), 6.85–7.45 (m, 8 H, aromatic), 12.95 (br s, 1 H, NH). Anal. ($C_{19}H_{14}ClN_3OS$) C, H, N.

***N*-[4-(2-Benzoyl-4-chlorophenyl)-5-cyanothiazol-2-yl]acetamide (29).** A stirred mixture of 18 g (0.0492 mol) of **28**, 36 g (0.12 mol) of sodium dichromate, and 540 mL of AcOH was refluxed under a drying tube for 15 h. The mixture was poured, with stirring, into 1200 mL of ice–water to give a light green solid. After filtering, the solid was washed with H_2O and air-dried on the funnel to give 14.7 g of crude **29**. The mixture was chromatographed over silica gel and eluted first with 2% AcOEt in CH_2Cl_2 and then with 10% AcOEt in CH_2Cl_2 to give 3.2 g of starting material and 5.1 g (27%) of **29**. Recrystallization of a sample from ether/petroleum ether gave white plates: mp 228–230 °C; IR (KBr) 3235, 3170, 2215, 1674, 1663, 1545 cm^{-1}; UV max (EtOH) 237 nm (ϵ 29 600), 254 (31 400), 285 (sh, 11 500), 315 (sh, ϵ 6800); NMR (Me_2SO-d_6) δ 2.15 (s, 3 H, CH_3), 7.25–7.85 (m, 8 H, aromatic), 12.76 (br s, 1 H, NH); MS, m/e 381 (M^+). Anal. ($C_{16}H_{12}ClN_3O_2S$) C, H, N.

***N*-(8-Chloro-6-phenyl-4*H*-thiazolo[5,4-*d*][2]benzazepin-2-yl)acetamide (30).** A mixture of 3.1 g (0.008 mol) of **29**, Raney nickel (2 teaspoonfuls), and 125 mL of EtOH was shaken with hydrogen at 18 psi for 2 h. After the mixture was filtered to remove the catalyst, the filtrate was concentrated in vacuo to give 2.6 g of **30** as a gum. Crystallization from a small amount of EtOH gave 1.1 g (37%) of nearly white crystals. Recrystallization of a sample from EtOH gave **30** as white microneedles: mp 270–274 °C dec; IR (KBr) 3400, 3325, 1692, 1675, 1652, 695; UV max (EtOH) 228 nm (ϵ 57 700), 276/7 (24 960), 340 (3670); NMR (Me_2SO-d_6) δ 2.17 (s, 3 H, CH_3), 4.41 (s, 2 H, CH_2), 7.30–8.03 (m, 8 H, aromatic), 12.25 (br s, 1 h, NH); MS, m/e 367 (M^+). Anal. ($C_{19}H_{14}ClN_3OS$) C, H, N.

8-Chloro-6-phenyl-4*H*-thiazolo[5,4-*d*][2]benzazepin-2-amine (17), from 30. A stirred suspension of 0.6 g (0.00164 mol) of powdered **30**, in 10 mL of 2 N NaOH, was heated at reflux under argon for 1 h. The mixture was cooled and filtered. The off-white solid was washed with H_2O and air-dried to give 0.5 g of **17**. Pure product (0.25 g, 47%) was obtained after preparatory chromatography, followed by crystallization from Et_2O. Recrystallization from EtOH/CH_2Cl_2 solution gave pale yellow prisms: mp 244–246 °C dec; MS, m/e 325 (M^+). Anal. ($C_{17}H_{12}ClN_3S$) C, H, N.

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Registry No. 1, 76049-52-0; 2, 76049-53-1; 3, 76049-54-2; 4, 76049-60-0; 5, 78367-94-9; 6, 78367-91-6; 7, 78367-92-7; 8, 78367-93-8; 9, 78367-95-0; 10, 78379-98-3; 11, 78367-96-1; 12, 78367-98-3; 13, 78367-99-4; 14, 78367-97-2; 15, 78368-00-0; 16, 78368-01-1; 17, 78368-02-2; 18, 78379-99-4; 19, 78368-04-4; 20, 78368-03-3; 21, 78368-05-5; 22, 21143-54-4; 23, 81992-91-8; 24, 21143-53-3; 25, 83562-01-0; 26, 83562-02-1; 27, 83562-03-2; 28, 83562-04-3; 29, 83562-05-4; 30, 83562-06-5; CH_3NH_2, 74-89-5; thioacetamide, 62-55-5; thiourea, 62-56-6.

(8) Prepared by reduction of 2-benzoyl-4-chlorobenzophenone.