cm^{-1}; MS, m/e (rel intensity) 153 (M^+, 8.0), 124 (3.3), 111 (11.5), 97 (25.0), 96 (100.0), 95 (22.4). Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.54; H, 9.88; N, 9.11.

3,6-Dihydro-6-(3-((tetrahydro-2*H*-pyran-2-yl)oxy)-propyl)-2(1*H*)-pyridinone (33). Organolithium reagent **8** was generated by adding 2-(3-chloropropoxy)tetrahydro-2*H*-pyran (116.74 g, 0.65 mol) in Et_2O (100 mL) over 3.5 h to Li (11.2 g 1.6 mol) in Et_2O (150 mL) at -10 °C. After an additional 1 h, the reaction was titrated with diphenylacetic acid, and the organolithium concentration was 1.25 mol (57%). In a separate flask pyridinone (**31**) (17.8 g, 0.187 mol) and THF (100 mL) were cooled to -78 °C. The organolithium reagent **8** was added to the pyridinone in 1 portion. The reaction was warmed to room temperature and stirred overnight. The deep orange solution was quenched by pouring over ice (400 g). The aqueous layer was extracted with EtOAc (3 × 100 mL). The organic layers were combined, extracted with saturated aqueous NaCl, dried, and evaporated in vacuo to 72.04 g of crude product. Under full vacuum (0.1 mm, 25-30 °C), 2-propoxytetrahydro-2*H*-pyran (33.24 g, 35%) was distilled from the product. The remaining material was chromatographed on the Waters' Prep-500 (SiO_2; CH_2Cl_2/MeOH (5%)) and 4 major fractions were isolated. Fraction 1 eluted at 1.5 column volumes and contained product (4.3 g). Fraction 2 eluted at 2.5 column volumes and contained a THP derivative (11.0 g). Fraction 3 eluted at 4.5 column volumes and contained a THP derivative with nitrogen in the moleucle (4.5 g). Fraction 4 eluted at >9 column volumes, when eluted with methanol, and contained material (16.0 g) which was not identifiable by NMR.

Fraction 1 was rechromatographed under similar conditions and pure **33** (2.09 g, 4.7%) was isolate: ^1H NMR ($CDCl_3$) δ 1.38-2.05 (m, 10 H, CH_2), 2.89-3.05 (m, 2 H, $OCCH_2$), 3.29-4.34 (m, 5 H, OCH_2, NCH), 4.65 (s, 1 H, OCHO), 5.80 (s, 2 H, CH=CH), 6.70 (brs, 1 H, NH); IR (neat) 3211, 3095, 3044, 2942, 1680, 1664, 1136, 1120, 1076, 1064, 1034, 1023 cm^{-1}; MS, m/e (rel intensity) 239 (M^+, 1.2), 191 (2.4), 184 (2.2), 155 (44.3), 154 (15.4), 138 (13.3), 121 (6.1), 96 (100.0), 85 (52.4). Anal. Calcd for $C_{13}H_{21}NO_3$ and 0.6% H_2O: C, 64.85; H, 8.86; N, 5.81. Found: C, 64.81; H, 9.24; N, 5.90.

Fraction 2 was rechromatographed under similar conditions, and 7.37 g of purer material was isolated: ^1H NMR ($CDCl_3$) δ 1.30-2.00 (m, 14 H), 2.68 (s, 1 H), 3.20-4.00 (m, 6 H), 4.60 (s, 1 H); ^{13}C NMR ($CDCl_3$) ppm 99.0 (d), 71.5 (d), 71.4 (d), 67.9 (t), 62.6 (t), 62.5 (t), 37.0 (t), 34.8 (t), 32.6 (t), 30.7 (t), 26.3 (t), 26.1 (t), 25.4 (t), 21.9 (t), 19.6 (t); IR (neat) 3386, 2940, 2867, 1643, 1353, 1200, 1138, 1121, 1077, 1060, 1033, 1024, 989, 974, 907, 869 cm^{-1}; ash, 0.15%; water content, 0.25%. Anal. Found for C and H: C, 62.06; H, 10.21. This material resembles the THP derivative of 1,6-hexanediol, prepared independently,[27] by ^1H NMR, but by ^{13}C NMR and TLC the material is clearly different.

Fraction 3 was rechromatographed under similar conditions, and 640 mg of purer material was isolated: ^1H NMR ($CDCl_3$) δ 1.35-2.20 (m, 10 H), 2.35-2.80 (m, 3 H), 3.40-4.20 (m, 5 H), 4.65 (s, 1 H), 6.00 (d, 1 H, J = 6.6 Hz), 7.21 (d, 1 H, J = 6.6 Hz); IR (neat) 3412, 3276, 3133, 3057, 3025, 2939, 2862, 1642, 1627, 1574, 1154, 1137, 1120, 1074, 1065, 1034, 1021, 1004, 987 cm^{-1}; MS, m/e (rel intensity) 239 (M^+, 21.8), 222 (15.9), 208 (9.9), 195 (34.5), 180 (14.5), 167 (82.5), 148 (28.7), 127 (21.6), 85 (100.0). Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.24; H, 8.85; N, 5.85. Found: C, 66.56; H. 9.25; N. 4.28. This material was thought to be the α,β-unsaturated isomer of **33** due to MS and IR data. However, the elemental analysis and NMR were not consistent with this structure.

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Registry No. **1**, 101773-62-0; **2**, 50720-19-9; **3**, 101773-63-1; **6**, 1628-89-3; **7**, 101773-64-2; **8**, 92785-46-1; **9**, 101773-65-3; **10**, 101773-66-4; **11**, 101773-67-5; **12**, 101773-68-6; **13**, 101773-69-7; **14**, 85560-51-6; **15**, 101773-70-0; **16**, 101773-71-1; **17**, 101773-72-2; **18**, 101773-73-3; **19**, 101773-74-4; **20**, 101773-75-5; **21**, 101773-76-6; **24**, 101773-77-7; **25**, 101773-85-7; **26**, 101773-78-8; **27**, 101773-79-9; **28**, 101773-80-2; **29**, 101773-81-3; **30**, 101773-82-4; **31**, 142-08-5; **32**, 101773-83-5; **33**, 101773-84-6; *n*-BuLi, 109-72-8; 2-(3-chloropropoxy)tetrahydro-2*H*-pyran, 42330-88-1; 2-(5-chloropentoxy)-tetrahydro-2*H*-pyran, 13129-60-7; 3-chloro-1,1-diethoxypropane, 35573-93-4.

2-Benzazepines. 9.[1] Synthesis and Chemistry of 3*H*-2-Benzazepine and Pyrimido[4,5-*d*][2]benzazepine Derivatives

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The synthesis of 8-chloro-1-phenyl-3*H*-2-benzazepine analogues **6a-c** and their dihydro derivatives **9a-c** from the corresponding alkynes **1a-c** is discussed. The bromination followed by dehydrobromination of **6a-c** led to the formation of the corresponding 5-bromo-1-phenyl-3*H*-2-benzazepines **14a-c** which were useful synthetic intermediates in the synthesis of more complex 2-benzazepine derivatives. An example of the utility for the vinyl bromides **14a-c** in the synthesis of heterocyclic ring systems is presented. The palladium-catalyzed carbalkoxylation of **14a-c** led to a facile synthesis of pyrimido[4,5-*d*][2]benzazepine derivatives.

As part of a program aimed at the discovery of novel agents active on the central nervous system, syntheses of 2-benzazepine derivatives have been investigated in these laboratories[2,3] and elsewhere.[4] Both groups have employed the use of organometallic chemistry as the key step to produce efficient and practical syntheses of the 2-benzazepine ring system. The use of palladium-catalyzed coupling of substituted *o*-iodobenzophenones with *N*-propargylphthalimide provided a facile approach to 2-benzazepin-4-ones and -5-ones[5] by hydration of the aryl-

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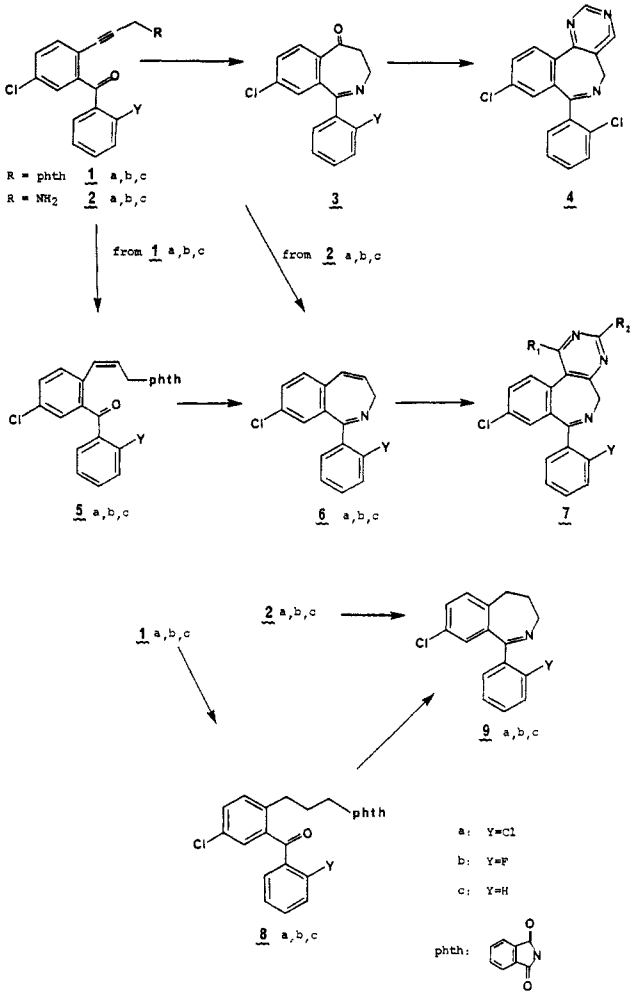
Scheme I



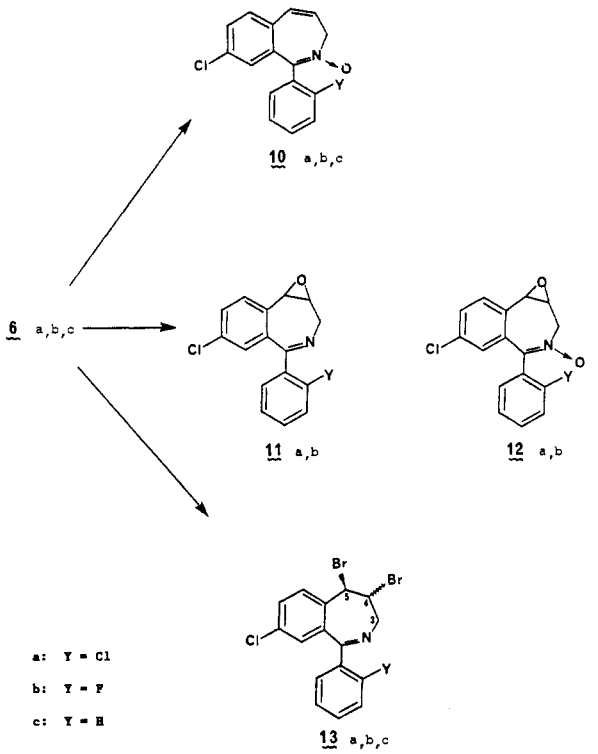
acetylene intermediates **1a–c** and **2a–c**. The resulting 2-benzazepin-5-ones **3** have served as synthetic intermediates in the synthesis of pyrimido[5,4-*d*][2]benzazepines.[2,3] One member from this series, **4**, was under development as an anxiolytic agent. In this paper, we discuss further chemistry of intermediates **1a–c** and **2a–c**, leading to the syntheses of 3*H*-2-benzazepine derivatives **6a–c** and the isomeric pyrimido[4,5-*d*][2]benzazepines **7**.

Results

The 3*H*-2-benzazepines **6a–c** were obtained by the partial hydrogenation of the acetylene functionality in **2a–c** over 10% palladium on barium sulfate in ethanol. The *cis*-olefin product spontaneously ring closed to the azepine ring by Schiff base formation (Scheme I). Reduction of the acetylene functionality of **1a–c** over the same catalyst followed by removal of the phthaloyl group from **5a–c** also gave **6a–c**. However, the overall yield from **1a–c** was lower than in the alternate sequence. In contrast, the formation of the dihydro derivative **9a–c** was best achieved first by catalytic reduction of the acetylene functionality in **1a–c** to **8a–c** followed by removal of the phthaloyl group using 40% aqueous methylamine. In the reduction of **2a–c** over Raney nickel, hydrogen absorption ceased before the desired reaction was complete, leading to mixtures of **6a–c** and **9a–c**.

The imine and the olefin groups in **6a–c** were both susceptible to electrophilic attack with the imine functionality being more reactive (Scheme II). Treatment of

Scheme II



6a–c with 1 equiv of *m*-chloroperoxybenzoic acid in methylene chloride gave the *N*-oxide derivatives **10a–c**. The use of an excess of *m*-chloroperoxybenzoic acid in the oxidation of **6a–c** or **10a–c** produced no reaction at the olefinic group. However, reaction of **6a,b** with the stronger peroxytrifluoroacetic acid,[6] under conditions in which the generated trifluoroacetic acid was not neutralized, led to the formation of a mixture of the epoxides **11a,b** and the epoxy *N*-oxides **12a,b**. In a similar manner, bromination of **6a–c** which yielded the dibromo compounds **13a–c** required the use of 2 equiv of bromine for complete reaction to occur. Treatment of the reaction mixture with aqueous sodium hydroxide, presumably to hydrolyze the iminium intermediates, was required prior to the isolation of **13a–c** from these reaction mixtures. If the hydrobromide salts of **6a–c** were prepared prior to the bromination, the use of only 1 equiv of bromine was necessary. These results imply that protonation of the basic imine nitrogen atom protects it from electrophilic attack and allows reaction to occur at the less reactive olefin site.

The dehydrobrominations of **13a–c** resulted in the syntheses of the vinyl bromides **14a–c**. Reaction of **13a–c** with potassium hydroxide (or potassium *tert*-butoxide) in a mixture of tetrahydrofuran and *tert*-butyl alcohol, which are conditions known to favor syn elimination,[7,8] led to **14a–c** in good yield (Table I, Scheme III). Byproducts in the preparation of **14a,b** were identified as the 2-benzazepines **6a,b** and the *tert*-butyl ethers **15a,b**. Changing the dehydrobromination conditions to sodium hydroxide (or sodium methoxide) in a mixture of dioxane and methanol, which are conditions favoring the anti reaction pathway,[7,8] led to significantly lower yields of **14a–c** and resulted in the formation of significant amounts of the methyl ethers **16a–c** (Table I).

The annulation of a pyrimidone ring at the 4,5-position of the 2-benzazepine ring provides an example of the utility

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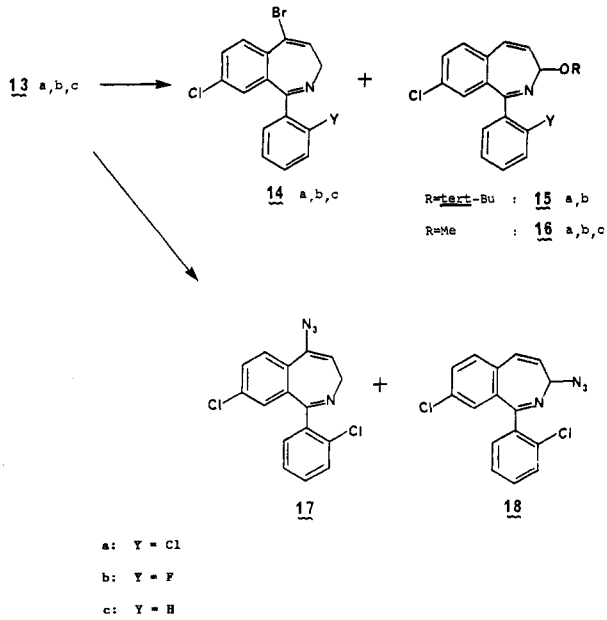
Table I. Dehydrobromination of 13a–c

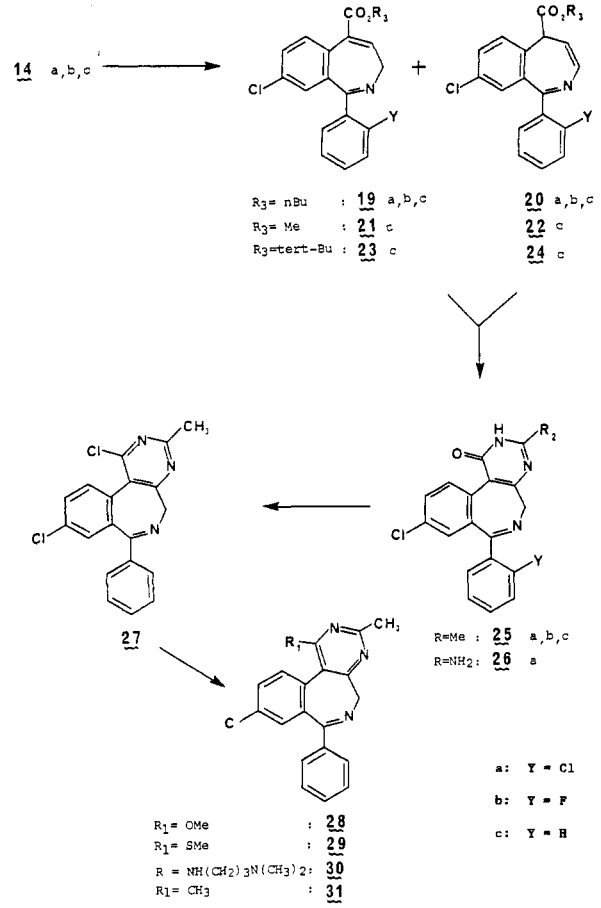
reaction				products[b]					
compd	Y	method[a]	reactn time, h	compd	yield, %	compd	yield, %	compd	yield, %
13a	Cl	A	3	**14a**	80 (46)	**15a**	9 (1)	**3a**	6 (1)
13b	F	A	1.25	**14b**	89 (70)	**15b**	4 (1)	**3b**	4 (1)
13c	H	A	1.25	**14c**	99 (86)				
13a	Cl	B	1.5	**14a**	19 (22)	**16a**	72 (64)		
13b	F	B	2.5	**14b**	41 (40)	**16b**	54 (42)		
13c	H	B	3.0	14c	78 (73)	**16c**	17 (12)		

[a] Method A: 10 mmol of **13a–c**, 20 mmol of KOH, 50 mL of *t*-BuOH, 10 mL of THF, room temperature; method B: 10 mmol of **13a–c**, 75 mmol of NaOH, 50 mL of MeOH, 10 mL of dioxane. [b] Yield determined by HPLC. Isolated yield in parentheses.

Scheme III



Scheme IV



of the vinyl bromide functionality in the synthesis of heterocycles.[9] The palladium(0)-catalyzed carbalkoxylation[10] and coupling reactions[11] of vinyl bromides **14a–c** were explored (Scheme IV). Reaction of **14a–c** with 1-butanol and carbon monoxide at 50 psi in the presence of palladium bis(triphenylphosphine)dibromide and cuprous iodide resulted in a mixture of the isomeric *n*-butyl esters **19a–c** and **20a–c**. Methanol and *tert*-butyl alcohol were substituted for 1-butanol in the carbalkoxylation of **14c** and provided mixtures of the crystalline methyl esters **21c** and **22c** and the *tert*-butyl esters **23c** and **24c**. These crystalline compounds were used to characterize the carbalkoxylation reaction products. The higher boiling 1-butanol was employed when the mixture of esters was used in a further reaction. This protocol of employing 1-butanol was adopted to avoid elevated reaction pressures which occur when the reaction temperature exceeded the boiling point of the alcohol. However, any ester could be prepared by using this procedure from the vinyl bromide and the appropriate alcohol.

Cuprous iodide catalytically facilitates the palladium-catalyzed coupling of aryl iodides and acetylenes[12] and stoichiometrically participates in the palladium-catalyzed oxidation of olefins to carbonyl groups.[13] The addition of 2 to 4 mol % of cuprous iodide to the carbalkoxylation reaction significantly reduced the reaction time (18 h to 3 h). The function of the cuprous iodide was not clear but may involve either the reduction of the palladium(II) salt[14] or the mediation of copper (possibly copper(0)) as a transmetalating agent of the vinyl moiety to palladium.[15]

Reaction of the crude mixture **19a,c** and **20a,c** with acetamidine, and of **19b** and **20b** with acetamidine or guanidine, produced the dihydropyrimido[4,5-*d*][2]benzazepines which were not isolated but oxidized with manganese dioxide to give the pyrimido[4,5-*d*][2]benzazepinones **25a–c** and **26b**. Both esters were used in the

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(11) To be described elsewhere.

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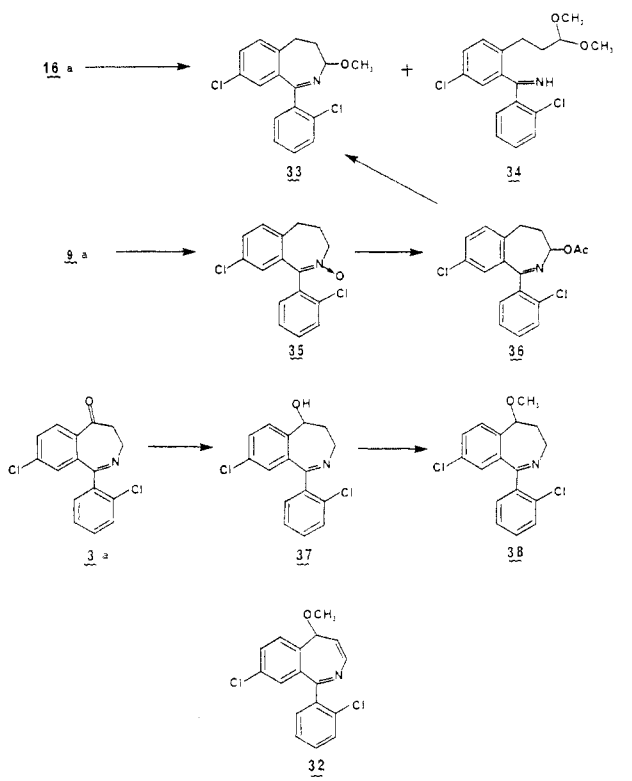
(15) For a discussion of transmetalation reactions, see: Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*, Kelly, A., Ed.; University of Science Books: Mill Valley, CA, 1980; pp 571–576.

Scheme V



reaction since **20a–c** was shown to isomerize into **19a–c**. Treatment of **25c** with phosphorus oxychloride produced the chloro derivative **27c** which served as a convenient intermediate for the preparation of 1-substituted pyrimido[4,5-*d*][2]benzazepine derivatives **28–31** by nucleophilic displacement.

The dehydrobromination of **13a–c** to give **14a–c** was the lowest yield step in the synthesis of the pyrimidobenzazepines and thus required improvement. Before the dehydrobromination was thoroughly studied, an alternate structure, **32** was considered for the methyl ether **16a**. That the structure of **16a**, and by analogy the methyl ethers **16b,c** and the *tert*-butyl ethers **15a,b**, was as indicated was shown by conversion of **16a** to the methyl ether **33** (Scheme V). This transformation was effected by reduction of the olefinic group of **16a** over Raney nickel. The same compound was prepared independently from benzazepine **9a**. Oxidation of **9a** with *m*-chloroperoxybenzoic acid gave *N*-oxide **35** which was refluxed in acetic anhydride to afford **36** in a Polonovsky-type rearrangment.[18] Treatment of **36** with methanolic methanesulfonic acid gave a mixture of **33** and the acetal **34**, which were easily separated and identified. The reduced form of the alternate structure **32**, compound **38**, was also synthesized (Scheme V) and was shown to be different from compound **16a**. Reduction of **3a** with sodium borohydride gave the alcohol **37**. Methylation of **37** by reaction with lithium diisopropylamide in tetrahydrofuran and then by the addition of methyl iodide afforded compound **38**.

The mechanism for the formation of the vinyl bromides **14a–c** and the 3-alkoxy ethers **15a,b** and **16a,c** provided the clue for the optimization of the reaction conditions.

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(17) For examples of lithium halide displacements, see: Meyers, A. *J. Org. Chem.* **1971**, *36*, 3044. Buchta, E.; Merk, W. *Liebigs Ann. Chem.* **1968**, *716*, 106.

(18) Deslonchamps, P. *Stereoelectronic Effects in Organic Chemistry*, Organic Chemistry Series, Vol. 1; Pergamon: New York, 1983; Chapter 6.

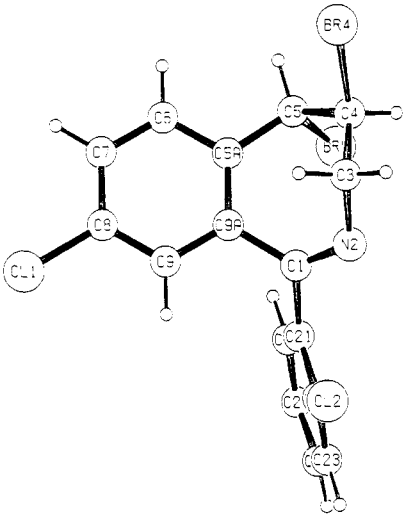


Figure 1. Perspective drawing of a molecule of **13a**. The A ring is 12° out of the plane of the paper. Cl(2) is above the plane of the paper, close to the viewer.

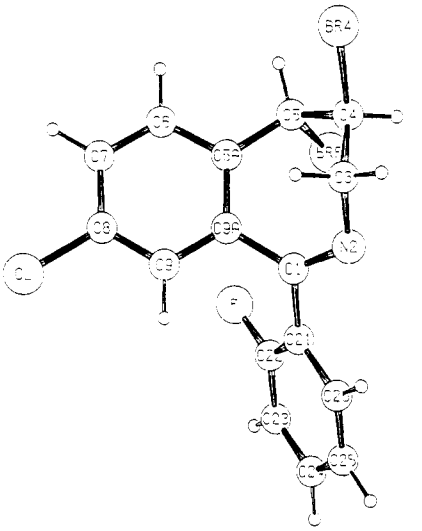


Figure 2. Perspective drawing of a molecule of **13b**. The A ring is 12° out of the plane of the paper. The fluroine atom is below the plane of the paper, away from the viewer.

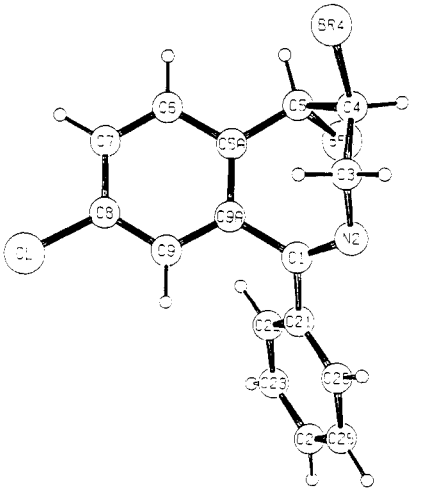
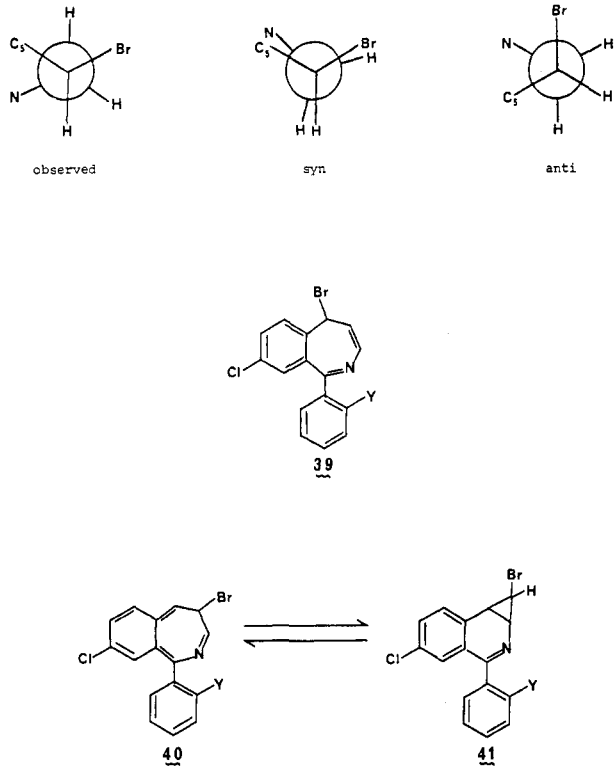


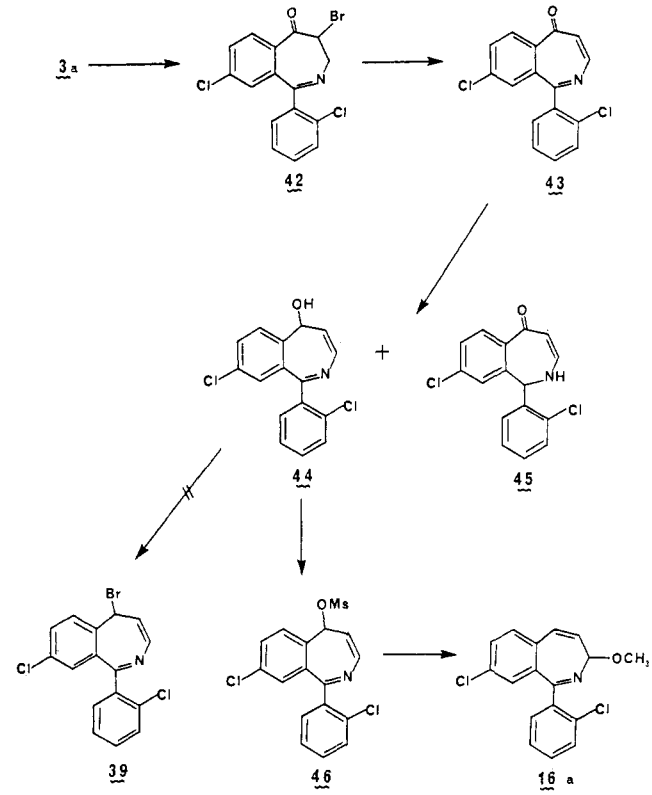
Figure 3. Perspective drawing of a molecule of **13c**. The A ring is 12° out of the plane of the paper.

The trans diaxial relationship of the bromines in **13a–c** (see Figures 1–3) and the constraint of the azepine ring required a syn elimination of HBr in order to form **14a–c**. An anti elimination of HBr to give **14a–c** would necessitate

Scheme VI



Scheme VII



an inversion of one of the bromines prior to the elimination. This process, albeit unlikely, was suggested by the formation of the vinyl azide **17** in good yield (with minor amounts of **18**) by the reaction of **13a** with sodium azide in dimethyl sulfoxide (Scheme III). The formation of **17** was explained by the S_N2 displacement of the benzylic bromide by azide with inversion followed by a trans elimination of HBr from the 4- and 5-positions. Treatment of **13a** with lithium or sodium bromide and sodium carbonate[17] in methanol at reflux or dimethyl sulfoxide at room temperature for 24 h produced no change in the starting material. The lack of reaction suggested that inversion of one of the bromines in the dihydrobromination was not involved in the reaction.

Ethers **15a,b** and **16a–c** were not formed in any appreciable amount through the corresponding vinyl bromides but were formed by a separate process. This assumption was tested by treatment of **14a** with sodium hydroxide in methanol and resulted in the formation of only 0.5% of the corresponding ether **16a** after 1.5 h (the duration of the dehydrobromination reaction) and 3% after 3 days. The mechanism for the formation of ethers **15a,b** and **16a–c** may involve first the removal of a proton from the 3-position of **13a–c** followed by one of two pathways. Pathway a requires the elimination of the bromine atom from the 3-position by either a syn or an anti elimination. In either case, from the inspection of models and the X-ray structures of **13a–c**, the bromine atom at the 4-position is gauche to both of the protons at the 3-position. The azepine ring therefore must undergo a conformational change to allow these atoms to either eclipse each other for a syn elimination or be antiperiplanar for an anti elimination (Scheme VI). Either of these eliminations will afford the 5*H*-2-benzazepine intermediate **39** which is attacked by the alcohol in an S_N2' fashion to give the corresponding ether. Pathway b is based on the antiperiplanar relationship[18] of the proton at the 3-position and the bromine at the 5-position of **13a–c** as observed both in the crystalline state (Figure 1) and in solution (from NMR coupling constants). Elimination of HBr from these positions would generate the 4*H*-2-benzazepine intermediate **40** which can ring close in a concerted manner to the cycloprop[*c*]isoquinoline **41**[19,20] in which the bromine atom is endo. Solvolysis of **41**, with *tert*-butyl alcohol or methanol leads in the formation of ethers **15a,c** and **16a–c**, respectively. The solvolysis of cyclopropyl tosylates leading to allylic alcohols and ethers is well documented[21] and an example of the ring opening of cycloprop[c]isoquinoline with *tert*-butyl alcohol at the 1a carbon atom has been reported.[22]

There was literature precedence for pathway b (see above) but there was no evidence for pathway a. To test the viability of this hypothetical pathway, the synthesis of intermediate **39** was investigated (Scheme VII). Bromination of the hydrobromide salt of **3c**[5] in methylene chloride gave the monobrominated product **42**. Elimination of HBr from **42** with triethylamine gave the benzazepinone **43**. Both of these reactions could be carried out in one pot or separately, in high yield. Reduction of **43** with lithium aluminum hydride at −78 °C gave a mixture of two products **44** and **45** in which **45** was the major product. Treatment of **44** with either triphenylphosphine dibromide[23] in methylene chloride or phosphorous tri-

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Table II. Crystal Data for 13a-c

	compound		
	13a	13b	13c
formula	$C_{16}H_{11}Br_2Cl_2N$	$C_{16}H_{11}Br_2ClFN$	$C_{16}H_{12}Br_2ClN$
formula wt	447.98	431.53	413.54
crystal system	monoclinic	orthorhombic	monoclinic
space group	$C2/c$	$Pcab$	$P2_1/c$
a (Å)	28.990 (6)	12.291 (2)	12.923 (3)
b (Å)	8.001 (3)	15.699 (2)	18.016 (4)
c (Å)	16.060 (3)	16.402 (2)	6.740 (2)
β (deg)	116.13 (1)		91.29 (2)
Z	8	8	4
d_{calcd} (g cm^{-3})	1.779	1.811	1.751
μ(Cu Kα) (cm^{-1})	97.0	88.1	87.5

bromide and pyridine[24] in methylene chloride led to the rapid consumption of starting material and the formation of highly colored reaction mixtures. Attempted purification of the reaction mixtures did not lead to the isolation of a product which could be identified as the 4*H*-2-benzazepine **39**. The inability to isolate **39** can be rationalized by its ionization to a benzotropylium ion in a similar manner to bromocycloheptatriene,[25] the proposed intermediate. Mesylate **46** was prepared under conditions milder than those used to generate **39** and provided the desired 5*H*-2-benzazepine ring system with a leaving group comparable to that of bromine. Reaction of **44** with methanesulfonyl chloride in the presence of triethylamine at −5 °C for 10 min (until there was no **44** detectable by TLC) was followed by cooling of the reaction mixture to −78 °C. The solution of **46** was treated with an excess of methanolic sodium hydroxide or added by cannula to a solution of methanolic sodium hydroxide. In both experiments, the methyl ether **16a** was the only product isolated.

The ortho substituent on the 1-phenyl group in **14a–c** determines the amount of ether **15a,b** and **16a–c** observed in the dehydrobromination reactions of **13a–c**. The fluorine substituent and to a greater extent the chlorine inductively increased the acidity of the protons at the 3-position of the azepine ring compared to hydrogen. The increased acidity of the 3-position protons increases the likelihood of their removal relative to the proton at the 5-position used in the syn elimination. The anion at the 3-position utilizes reaction pathway a and/or b to give the ether **15a,b** or **16a–c**.

The formation of the vinyl bromides **14a–c** proceeds by a syn elimination of HBr from the 4,5-positions of the azepine ring. The increased formation of **14a–c** at the expense of the corresponding ether when the base was changed from sodium to potassium hydroxide substantiates the syn elimination hypothesis.[7,8]

In summary, a facile method for the syntheses of the 3*H*-2-benzazepine and the pyrimido[4,5-*d*][2]benzazepine ring systems has been presented. In addition, the coupling of a propargylic amine with an aromatic iodide followed by either a partial or complete reduction of the acetylene group provides a mild method for the attachment of *cis*-propenamine or propanamine side chains to an aromatic ring. This three-step procedure for the attachment of a *cis*-propenamine to an aromatic ring is complementary to the reported method for the introduction of a *trans*-propenamine side chain.[26]

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Crystallography. All intensity data were measured on a Higler-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination). The crystal data are given in Table II. A multiple solution procedure was used to solve the three structures (Figures 1, 2, and 3). Experimental details are submitted as supplementary material as indicated at the end of this paper.

Experimental Section

Melting points were determined on a Thomas Hoover apparatus and are uncorrected. NMR spectra were recorded on Varian T-60 and HA-100 instruments and are reported in parts per million from internal Me_4Si. Infrared and mass spectra (MS) were recorded on Perkin-Elmer 137 and CEC-110B instruments, respectively. Normal phase high performance liquid (HPLC) was carried out on either an ES-SIL 10-cm AI21 or an ES 3UM A121 column using EtOAc/heptane (5:95 v/v) as eluent. Merck silica gel 60, mesh 230–400, was used for all column chromatography separations. Anhydrous sodium sulfate was used for drying of organic solvents.

8-Chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine Hydrobromide (6a). A mixture of 30.4 g (0.1 mol) of **2a**[5] and 1.2 g of 10% palladium on barium sulfate in a mixture of 50 mL of THF and 250 mL of EtOH was hydrogenated at room temperature and at atmospheric pressure until 2.3 L of hydrogen was absorbed. The catalyst was removed by filtration and the filtrate was diluted with 15 mL of 48% aqueous HBr and concentrated in vacuo. The residue crystallized from *i*-PrOH to give 34 g (92%) of **6a** as a yellow solid. Recrystallization from MeOH/ether gave **6a** as yellow prisms: mp 219–230 °C dec; IR (KBr) 2630 (NH), 1635 (C=N) cm^{-1}; NMR (Me_2SO-d_6) δ 4.07 (br d, J = 7 Hz, 2, C_3H), 6.47 (dt, J = 9.7 Hz, 1 C_4H), 7.29 (s, 1, Ar H), 7.35 (d, J = 9 Hz, 1, C_5H), 7.5–8.1 (m, 6, Ar H). Anal. Calcd for $C_{16}H_{12}BrCl_2N$: C, 52.06; H, 3.28; N, 3.80. Found: C, 51.80; H, 3.07; N, 3.69.

The free base of **6a** was prepared by partitioning the salt between a mixture of CH_2Cl_2 and saturated aqueous $NaHCO_3$. The CH_2Cl_2 solution was dried and concentrated in vacuo. The residue crystallized from ether to give the free base of **6a** as cream colored prisms: mp 117–118 °C; IR ($CHCl_3$) 1612 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.83 (d, J = 6 Hz, 2, C_3H), 6.30 (dt, J = 10, 6 Hz, 1 C_4H), 6.83 (d, J = 10 Hz, 1 C_5H), 7.1–7.6 (m, 7, Ar H); mass spectrum, m/e 286 (M^+ − H). Anal. Calcd for $C_{16}H_{11}Cl_2N$: C, 66.68; H, 3.85; N, 4.86. Found: C, 66.94; H, 3.92; N, 4.93.

8-Chloro-1-(2-fluorophenyl)-3*H*-2-benzazepine Hydrobromide (6b). Compound **6b** was prepared in the same manner as the preparation of **6a** to give the hydrobromide salt of **6b** (68%) as cream colored plates: mp 248–250 °C; IR (KBr) 2600 (NH); 1630 (C=N) cm^{-1}; NMR (Me_2SO-d_6) δ 4.02 (d, J = 6 Hz, 2, C_3H), 6.45 (dt, J = 10, 6 Hz, 1, C_4H), 7.25 (d, J = 10 Hz, 1, C_5H), 7.4–8.0 (m, 8, Ar H, NH). Anal. Calcd for $C_{16}H_{12}BrClFN$: C, 54.49; H, 3.43; N, 3.97. Found: C, 54.80; H, 3.39; N, 3.99.

The free base of **6b** was colorless prisms: mp 87–88 °C; IR ($CHCl_3$) 1612 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.80 (d, J = 6 Hz, 2 C_3H), 6.25 (dt, J = 10, 6 Hz, 1, C_4H), 6.77 (d, J = 10 Hz, 1, C_5H), 6.7–7.6 (m, 7 Ar H); mass spectrum, m/e 271 (M^+). Anal. Calcd for $C_{16}H_{11}ClFN$: C 70.72; H, 4.08; N, 5.16. Found: C, 70.99; H, 3.85; N, 5.13.

8-Chloro-1-phenyl-3*H*-2-benzazepine Hydrobromide (6c). Compound **6c** was prepared in the same manner as the preparation of **6a** to give **6c** (92%) as tan prisms: mp 252–264 °C dec; IR (KBr) 2630 (NH), 1622 (C=N) cm^{-1}; NMR (Me_2SO-d_6) δ 4.0 (br s, 2, C_3H), 6.48 (dt, J = 10, 6 Hz, 1 C_4H), 7.30 (d, J = 10 Hz, 1 C_5H), 7.44 (d, J = 2 Hz, 1, Ar H), 7.5–8.1 (m, 7, Ar H). Anal. Calcd for $C_{16}H_{13}BrClN$: C, 57.42; H, 3.91; N, 4.21. Found: C, 57.23; H, 3.91; N, 4.44.

1-[4-Chloro-2-(chlorobenzoyl)phenyl]-3-phthalimidopropene (5a). A mixture of 26.1 g (10 mmol) of **1a** and 0.5 g of prehydrogenated Pd/$BaSO_4$ in 150 mL of THF was hydrogenated at room temperature and atmospheric pressure until 1.6 L of hydrogen was absorbed (2 h). The catalyst was removed by filtration and the solution was concentrated in vacuo. The residue was triturated with ether to give 17.8 (67%) of **5a** as a colorless solid. Recrystallization from ether gave **5a** as colorless crystals: mp 90–92 °C; IR ($CHCl_3$) 1780, 1725 (imide C=O), 1685 (ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.33 (dd, J = 2, 6 Hz, CH_2), 5.68

(dt, J = 11, 7 Hz, 1, Ch), 6.74 (dt, J = 2, 11 Hz, 1, CH), 7.2–8.0 (m, 11, Ar H); mass spectrum, m/e 435 (M^+). Anal. Calcd for $C_{24}H_{15}Cl_2NO_3$: C, 66.07; H, 3.47; N, 3.21. Found: C, 65.88; H, 3.77; N, 3.32.

1-[4-Chloro-2-(fluorobenzoyl)phenyl]-3-phthalimidopropene (5b). Compound **5b** was prepared in the same manner as the preparation of **5a** to give **5b** (70%) as colorless needles: mp 117–118 °C; IR ($CHCl_3$) 1772, 1715 (imide C=O), 1670 (ketone C=O), and 1612 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 4.33 (dd, J = 7, 11.5 Hz, 1, CH), 5.63 (dt, J = 7, 11.5 Hz, 1, CH), 6.61 (dt, J = 2, 11.5 Hz, 1, CH), 6.9–7.9 (m, 11, Ar H); mass spectrum, m/e 421 (M^+). Anal. Calcd for $C_{24}H_{15}ClFNO_3$: C, 68.66; H, 3.60; N, 3.34. Found: C, 68.70; H, 3.47; N, 3.21.

1-(4-Chloro-2-benzoylphenyl)-3-phthalimidopropene (5c). Compound **5c** was prepared in the same manner as the preparation of **5a** to give **5c** (60%) as colorless prisms: mp 70–72 °C; IR ($CHCl_3$) 1776, 1715 (imide C=O), 1670 (ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 4.35 (dd, J = 2, 8 Hz, 2, CH_2), 5.61 (dt, J = 6, 12 Hz, 1, CH), 6.51 (dt, J = 2, 12 Hz, 1, CH), 7.3–7.9 (m, 12, Ar H); mass spectrum, m/e 401 (M^+). Anal. Calcd for $C_{24}H_{16}ClNO_3$: C, 71.74; H, 4.01; N, 3.49. Found: C, 71.66; H, 3.95; N, 3.38.

1-[4-Chloro-2-(chlorobenzoyl)phenyl]-3-phthalimidopropane (8a). A mixture of 40 g (91 mmol) of **1a**[5] and a teaspoonful of Ranel nickel[28] in 400 mL of THF was hydrogenated at room temperature and atmospheric pressure. When 4.5 L of hydrogen was absorbed, the catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was crystallized from ether to give 32 g (75%, mp 110–112 °C) of **8a** as a pale yellow solid. Recrystallization from CH_2Cl_2/ether gave **8a** as colorless prisms: mp 115–117 °C; IR ($CHCl_3$) 1770, 1712 (imide C=O), 1677 (ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.01 (quintet, J = 7 Hz, 2 CH_2), 2.90 (t, J = 7 Hz, 2, CH_2), 3.73 (t, J = 7 Hz, 2, CH_2), 7.2–7.9 (m, 11, Ar H); mass spectrum, m/e 437 (M^+). Anal. Calcd for $C_{24}H_{17}Cl_2NO_3$: C, 65.76; H, 3.91; N, 3.19. Found: C, 65.76; H, 3.90; N, 3.13.

1-[4-Chloro-2-(2-fluorobenzoyl)phenyl]-3-phthalimidopropane (8b). Compound **8b** was prepared in the same manner as the preparation of **8a** to give **8b** (79%) as cream colored prisms: mp 99–100 °C; IR ($CHCl_3$) 1775, 1715 (imide C=O), 1675 (ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.90 (m, 2, CH_2), 2.79 (m, 2, CH_2), 3.67 (t, J = 7 Hz, 2, NCH_2), 7.0–7.8 (m, 11, Ar H); mass spectrum, m/e 423 (M^+). Anal. Calcd for $C_{24}H_{17}ClFNO_3$: C, 68.33; H, 4.07; N, 3.32. Found: C, 68.43; H, 3.97; N, 3.44.

1-(4-Chloro-2-benzoylphenyl)-3-phthalimidopropane (8c). Compound **8c** was prepared in the same manner as the preparation of **8a** to give **8c** (89%) as pale yellow prisms: mp 98–99 °C; IR ($CHCl_3$) 1770, 1710 (imide C=O), 1665 (ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.92 (m, 2, CH_2), 2.64 (m, 2, CH_2), 3.61 (t, J = 7 Hz, 2, NCH_2), 7.2–7.8 (m, 12, Ar H); mass spectrum, m/e 403 (M^+). Anal. Calcd for $C_{24}H_{18}ClNO_3$: C, 71.38; H, 4.49; N, 3.47. Found: C, 71.50; H, 4.37; N, 3.48.

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3*H*-2-benzazepine (9a). A mixture of 31 g (71 mmol) of **8a** and 50 mL of 40% aqueous methylamine in 100 mL of ethanol was stirred at room temperature for 6 h. The mixture was diluted with 500 mL of water and extracted with ether. The ether solution was washed with water, dried, and concentrated in vacuo to dryness. The residue was purified by column chromatography (SiO_2, 300 g; eluent, CH_2Cl_2) to give 13.7 g (66%, mp 88–89 °C) of **9a** as a pale yellow solid. Recrystallization from petroleum ether gave **9a** as colorless crystals: mp 89–90 °C; IR ($CHCl_3$) 1610 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.39 (m, 2, CH_2), 2.76 (t, J = 7 Hz, 2, CH_2), 3.49 (t, J = 7 Hz, 2, CH_2), 6.89 (d, J = 2 Hz, 2 Ar H), 7.1–7.7 (m, 6, Ar H); mass spectrum, m/e 289 (M^+). Anal. Calcd for $C_{16}H_{13}Cl_2N$: C, 66.22; H, 4.52; N, 4.83. Found: C, 66.49; H, 4.55; N, 4.84.

8-Chloro-1-(2-fluorophenyl)-4,5-dihydro-3*H*-2-benzazepine Hydrochloride (9b). A mixture of 16.5 g (39 mol) of **8b** and 25 mL of 40% aqueous methylamine in 70 mL of ethanol was stirred at room temperature for 3 h. The mixture was diluted with 200 mL of water and extracted with ether. The ether solution was washed with water, dried, and concentrated in vacuo to dryness. The residue was diluted with 50 mL of 1.4 M methanolic HCl and further diluted with ether. The resulting precipitate was collected to give 9.2 g (71%) of **9b** as yellow crystals. Recrystallization from MeOH/ether gave **9b** as pale yellow plates: mp 209–215 °C; IR (KBr) 3400, 2450, 1727 (C=NH), 1630 (C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{14}Cl_2FN$: C, 61.95; H, 4.55; N, 4.52. Found: C, 62.15; H, 4.43; N, 4.46.

8-Chloro-1-(2-fluorophenyl)-4,5-dihydro-3*H*-2-benzazepine Hydrochloride (9b) from 2b. A mixture of 2.9 g (10 mmol) of **2b** and 1 g of Raney nickel in 50 mL of THF was hydrogenated at room temperature and atmospheric pressure. When 430 mL of hydrogen was absorbed, the catalyst was removed by filtration and the filtrate was concentrated at reduced pressure to dryness. The residue was dissolved in an excess of methanolic hydrogen chloride and diluted with ether to give a yellow solid. Recrystallization from MeOH/ether gave 1 g (33%) of **9b** as pale yellow plates: mp 210–214 °C. The mixture melting point with the material prepared from **8b** was not depressed.

8-Chloro-4,5-dihydro-1-phenyl-3*H*-2-benzazepine Hydrochloride (9c). Compound **9c** was prepared in the same manner as the preparation of **9a** to give **9c** (88%) as off-white crystals. Recrystallization from MeOH/ether gave **9c** as colorless needles: mp 234–235 °C; IR (KBr) 3450, 2450, 1930 (C=N H), 1620 (C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{15}Cl_2N$: C, 65.76; H, 5.17; N, 4.79. Found: C, 65.32; H, 5.23; N, 4.83.

8-Chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine 2-Oxide (10a). A solution of 2.4 g (8.4 mmol) of **6a** and 2.4 g (12 mmol) of 85% *m*-chloroperoxybenzoic acid in 100 mL of CH_2Cl_2 was stirred at room temperature for 1.5 h. The mixture was washed with 1 N aqueous NaOH and water, dried, and concentrated in vacuo to dryness. The residue crystallized from ether to give 2.2 g (87%, mp 213–214 °C) of **10a** as colorless crystals. Recrystallization from CH_2Cl_2/ether gave **10a** as cream colored prisms: mp 216–217 °C; NMR ($CDCl_3$) δ 4.56 (d, J = 7 Hz, 2, C_3H), 6.47 (dt, J = 10, 7 Hz, 1, C_4H), 6.96 (s, 1, Ar H), 7.04 (d, J = 10 Hz, 1, C_5H), 7.2–7.5 (m, 6, Ar H); mass spectrum, m/e 303 (M^+). Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.19; H, 3.65; N, 4.60. Found: C, 63.05; H, 3.50; N, 4.51.

8-Chloro-1-(2-fluorophenyl)-3*H*-2-benzazepine 2-Oxide (10b). Compound **10b** was prepared in the same manner as the preparation of **10a** to give **10b** (94%) as colorless prisms: mp 138–139 °C; NMR ($CDCl_3$) δ 4.50 (d, J = 7 Hz, 2, C_3H), 6.36 (dt, J = 10, 7 Hz, 1, C_4H), 7.05 (d, J = 10 Hz, 1, C_5H), 7.0–7.5 (m, 7, Ar H); mass spectrum, m/e 287 (M^+). Anal. Calcd for $C_{16}H_{11}ClFNO$: C, 66.79; H, 3.85; N, 4.87. Found: C, 66.71; H, 3.76; N, 4.72.

8-Chloro-1-phenyl-3*H*-2-benzazepine 2-Oxide (10c). Compound **10c** was prepared in the same manner as the preparation of **10a** to give **10c** (92%) as tan prisms: mp 122–123 °C; NMR ($CDCl_3$) δ 4.45 (d, J = 7 Hz, 2 C_3H), 6.37 (dt, J = 10, 7 Hz, 1, C_4H), 6.98 (d, J = 10 Hz, 1, C_5H), 7.2–7.6 (m, 7, Ar H); mass spectrum, m/e 269 (M^+). Anal. Calcd for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48; N, 5.21. Found: C, 71.35; H, 4.28; N, 5.11.

6-Chloro-4-(2-chlorophenyl)-1a,8b-dihydro-2*H*-oxireno[*d*][2]benzazepine (11a) and 6-Chloro-4-(2-chlorophenyl)-1a,8b-dihydro-2*H*-oxireno[*d*][2]benzazepine 3-Oxide (12a). A 1.2 M CH_2Cl_2 solution of peroxytrifluoroacetic acid (15 mL, 18 mmol) was added dropwise to a solution of the methanesulfonate salt of **6a**, mp 201–202 °C, in 25 mL of CH_2Cl_2 which was cooled to −20 °C. The mixture was stirred for 2 h at 0 °C. An additional 15 mL (18 mmol) of the 1.2 M CH_2Cl_2 solution of peroxytrifluoroacetic acid was added and the mixture was stirred for 2 h. The mixture was washed with saturated aqueous Na_2CO_3, dried, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 40 g; eluents, CH_2Cl_2 and then EtOAc/CH_2Cl_2 (1:9 v/v)) to give in the first product band 0.5 g (16%) of **11a** as a colorless oil which crystallized upon standing. Recrystallization from ether/petroleum ether gave **11a** as colorless crystals: mp 102–103 °C; IR ($CHCl_3$) 1625 (C=N) cm^{-1}; NMR (Me_2SO-d_6) δ 3.63 (dd, J = 2, 11 Hz, 1, C_3H), 3.84 (m, 1, C_4H), 4.05 (d, J = 4 Hz, 1, C_5H), 4.15 (dd, J = 6, 11 Hz, 1, C_3H), 6.78 (d, J = 2 Hz, 1, Ar H), 7.3–7.6 (m, 5, Ar H), 7.72 (d, J = 9 Hz, 1, Ar H); mass spectrum, m/e 303 (M^+). Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.17; H, 3.65; N, 4.60. Found: C, 63.20; H, 3.77; N, 4.55.

The second product band gave 1.3 g (41%) of **12a** as a colorless oil which crystallized upon standing. Recrystallization from ether gave **12a** as a colorless solid: mp 198–199 °C; NMR ($CDCl_3$) δ

(28) A high activity grade of Raney nickel similar to type 28 was used.

4.0–4.3 (m, 2, 2 CH), 4.3–4.6 (m, 2, 2 CH), 6.88 (br s, 1, Ar H), 7.2–7.7 (m, 7 Ar H); mass spectrum, *m/e* 319 (M^+). Anal. Calcd for $C_{16}H_{11}Cl_2NO_2$: C, 60.02; H, 3.46; N, 4.38. Found: C, 60.00; H, 3.52; N, 4.37.

6-Chloro-4-(2-fluorophenyl)-1a,8b-dihydro-2*H*-oxireno[*d*][2]benzazepine Hydrochloride (11b) and 6-Chloro-4-(2-fluorophenyl)-1a,8b-dihydro-2*H*-oxireno[*d*][2]benzazepine 3-Oxide (12b). A 1.2 M solution of peroxytrifluoroacetic acid in CH_2Cl_2 was prepared by the dropwise addition of 31 mL (0.23 mol) of trifluoroacetic acid anhydride to a mixture of 4.9 mL (0.19 mol) of 90% hydrogen peroxide in 125 mL of CH_2Cl_2 which was cooled to 0 °C. The CH_2Cl_2 solution of peroxytrifluoroacetic acid was added dropwise to a suspension of 54 g (0.15 mol) of the methanesulfonate salt of **6b**, mp 186–187 °C dec, in 525 mL of CH_2Cl_2 which was cooled to −30 °C. The mixture was stirred at 0 °C for 3 h. An additional 75 mL (0.09 mol) of the 1.2 M peroxytrifluoroacetic acid solution (prepared as above) was added and the resulting mixture was stirred overnight at 0 °C. The mixture was poured into an excess of saturated aqueous Na_2CO_3 and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with brine, dried, and concentrated in vacuo to dryness. The residue was purified by column chromatography (SiO_2, 400 g; eluents, CH_2Cl_2, 10% EtOAc in CH_2Cl_2 and 10% MeOH in CH_2Cl_2) to give in the 10% EtOAc/CH_2Cl_2 fraction 20 g of **11b** as a pale yellow oil. The oil was diluted with an excess of 1.4 M methanolic HCl and further diluted with ether. The resulting precipitate was collected by filtration to give 19.3 g (33%) of **11b** as colorless crystals: mp 134–136 °C; NMR (Me_2SO-d_6) δ 3.76 (d, J = 12 Hz, 1, C_3H), 4.12 (dd, J = 4, 6 Hz, 1, C_4H), 4.33 (d, J = 4 Hz, 1, C_5H), 4.42 (dd, J = 6, 12 Hz, 1, C_3H), 6.2–7.0 (br s, 1, NH), 7.21 (d, J = 2 Hz, 1, Ar H), 7.2–8.0 (m, 6, Ar H). Anal. Calcd for $C_{16}H_{11}ClFNO$: C, 59.28; H, 3.73; N, 4.32. Found: C, 58.91; H, 3.79; N, 4.22.

Further elution gave in the second product band 19.6 g (41%) of **12b** as colorless prisms: mp 161–162 °C; NMR (Me_2SO-d_6) δ 3.54 (dd, J = 2, 12 Hz, 1, C_3H), 3.83 (m, 1, C_4H), 4.02 (d, J = 4 Hz, 1, C_5H), 4.22 (dd, J = 5, 12 Hz, 1, C_3H), 6.91 (d, J = 2 Hz, 1, Ar H) 7.0–7.8 (m, 6, Ar H); mass spectrum, *m/e* 303 (M^+). Anal. Calcd for $C_{16}H_{11}ClFNO_2$: C, 63.27; H, 3.65; N, 4.61. Found: C, 63.16; H, 3.68; N, 4.59.

8-Chloro-1-(2-chlorophenyl)-4,5-dibromo-4,5-dihydro-3*H*-2-benzazepine (13a). Bromine (14.0 mL, 256 mmol) was added dropwise to a mixture of 75.2 g (203 mmol) of **6a** in 1 L of CH_2Cl_2. The solution was stirred at room temperature for 19 h. The mixture was washed with 250 mL of 3 N NaOH, dried, and concentrated in vacuo. The residue was crystallized from ether/petroleum ether to give 64.3 g (70%, mp 139–140 °C) as a yellow solid. Recrystallization from ether gave **13a** as pale yellow prisms: mp 139–141 °C; IR ($CHCl_3$) 1619 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.28 (dd, J = 9, 12 Hz, 1, C_3H), 4.23 (dd, J = 5, 12 Hz, 1, C_3H) 5.05 (m, 1, C_4H), 5.39 (d, J = 4 Hz, 1, C_5H), 7.0 (s, 1, Ar H), 7.2–7.6 (m, 6 Ar H); mass spectrum, *m/e* 445 (M^+). Anal. Calcd for $C_{16}H_{11}Br_2Cl_2N$: C, 42.90; 2.48; N, 3.13. Found: C, 43.02; H, 2.48; N, 3.15.

8-Chloro-4,5-dibromo-4,5-dihydro-1-(2-fluorophenyl)-3*H*-2-benzazepine (13b). Compound **13b** was prepared in the same manner as the preparation of **13a** to give **13b** (60%) as colorless prisms: mp 102–103 °C; IR ($CHCl_3$) 1608 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.49 (t, J = 11 Hz, 1, C_3H), 4.34 (dd, J = 5, 11 Hz, 1, C_3H), 5.15 (ddd, J = 2, 5, 11 Hz, 1, C_4H), 5.40 (d, J = 2 Hz, 1, C_5H), 7.0–7.8 (m, 7, Ar H); mass spectrum, *m/e* 431 (M^+). Anal. Calcd for $C_{16}H_{11}BrClFN$: C, 44.53; H, 2.57; N, 3.25. Found: C 44.63; H, 2.62; N, 3.24.

8-Chloro-4,5-dibromo-4,5-dihydro-1-phenyl-3*H*-2-benzazepine (13c). Compound **13c** was prepared in the same manner as the preparation of **13a** to give **13c** as colorless prisms: mp 113–115 °C; IR ($CHCl_3$) 1608 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.43 (t, J = 11 Hz, 1, C_3H), 4.34 (dd, J = 5, 11 Hz, 1, C_3H), 5.14 (ddd, J = 2, 5, 11 Hz, 1, C_4H), 5.37 (d, J = 2 Hz, 1, C_5H), 7.2–7.7 (m, 8, Ar H). Anal. Calcd for $C_{16}H_{12}Br_2ClN$: C, 46.47; H, 2.93; N, 3.39. Found: C, 46.58; H, 2.89; N, 3.20.

5-Bromo-8-chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine (14a) and 8-Chloro-1-(2-chlorophenyl)-3-methoxy-3*H*-2-benzazepine (16a). A mixture of 4.4 g (10 mmol) of **13a**, 10 mL of dioxane, and 15 mL of MeOH was refluxed until solution was complete. The solution was cooled and diluted with 85 mL of MeOH. A 40% aqueous NaOH solution (7.5 mL, 75 mmol) was added dropwise to the MeOH solution which was stirred at room temperature for 1.5 h. The excess base was neutralized by the addition of 20 mL of 3 N aqueous HCl and the solution was concentrated in vacuo. The residue was extracted with ether. The ether solution was washed with water and dried, a 0.5-mL aliquot was removed for HPLC analysis, and the remainder of the solution was concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 50 g; eluents, CH_2Cl_2 and then ether/CH_2Cl_2 (1:20 v/v)) to give in the first product band 0.8 g (22%) of **14a** as a cream colored solid. Recrystallization from ether gave **14a** as colorless prisms: mp 125–127 °C; IR ($CHCl_3$) 1611 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.73 (br d, 2, C_3H), 6.68 (t, J = 7 Hz, 1, C_4H), 7.05 (d, J = 2 Hz, 1, Ar H), 7.1–7.6 (m, 3, Ar H), 7.83 (d, J = 8 Hz, 1, C_6H); mass spectrum, *m/e* 365 (M^+). Anal. Calcd for $C_{16}H_{10}BrCl_2N$: C, 52.35; H, 2.75; N, 3.82. Found: C, 52.22; H, 2.56; N, 3.85.

The second product band gave 2.05 g (65%) of **16a** as cream colored needles: mp 83–85 °C; IR ($CHCl_3$) 1617 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.54 (s, 3, CH_3), 4.29 (dd, J = 2, 4 Hz, 1, C_3H), 6.15 (dd, J = 4, 11 Hz, 1, C_4H), 6.61 (dd, J = 2, 11 Hz, C_5H), 7.1–7.5 (m, 7, Ar H); mass spectrum, *m/e* 317 (M^+). Anal. Calcd for $C_{17}H_{13}Cl_2NO$: C, 64.17; H, 4.12; N, 4.40. Found: C, 64.26; H, 4.12; N, 4.32.

5-Bromo-8-chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine (14a) and 8-Chloro-1-(2-chlorophenyl)-3-(1,1-dimethylethoxy)-3*H*-2-benzazepine (15a). Powdered KOH was added to a well-stirred solution of 4.5 g (10 mmol) of **13a** and 10 mL of THF in 50 mL of *tert*-butyl alcohol in a water bath at room temperature. The mixture was stirred for 75 min, and the excess KOH was neutralized with the addition of 4 mL of 3 N aqueous HCl and concentrated in vacuo. The residue was extracted with ether. The ether solution was washed with water and dried, an aliquoit was removed for HPLC analysis, and the remainder of the solution was concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 50 g; eluents CH_2Cl_2 and then ether/CH_2Cl_2 (1:20 v/v)) to give in the first product band 1.7 g (46%) of **14a** as an off white solid. Recrystallization from ether gave **14a** as colorless prisms which were identical in every respect by mp, mmp, IR, MS, and NMR with an authentic sample.

The second product band gave 0.3 g of an oil which by TLC (SiO_2, EtOAc/petroleum ether (1:3 v/v)) was a mixture of two components. The oil was rechromatographed (SiO_2, 10 g; eluent EtOAc/petroleum ether (1:3 v/v)) to give in the first product 100 mg (3%) of **15a** as a colorless solid. Recrystallization from ether/petroleum ether gave **15a** as colorless prisms: mp 124–126 °C; IR ($CHCl_3$) 1605 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 1.28 (s, 9, 3 CH_3), 4.55 (dd, J = 2, 4 Hz, 1, C_3H), 6.22 (dd, J = 4, 10 Hz, 1, C4H), 6.64 (dd, J = 2, 10 Hz, 1, C_5H), 7.1–7.5 (m, 7, Ar H); mass spectrum, *m/e* 359 (M^+). Anal. Calcd for $C_{20}H_{21}Cl_2NO$: C, 66.68; H, 5.32; N, 3.89. Found: C, 66.78; H, 5.52; N, 3.82.

The second product band gave 100 mg (3%) of **6a** which was identical in every respect by mp, mmp, and NMR with an authentic sample.

5-Bromo-8-chloro-1-(2-fluorophenyl)-3*H*-2-benzazepine Hydrochloride (14b) and 8-Chloro-1-(2-chlorophenyl)-3-methoxy-3*H*-2-benzazepine Methanesulfonate Salt (16b). A mixture of 4.3 g (10 mmol) of **13b**, 10 mL of dioxane, and 15 mL of MeOH was heated to reflux until solution was complete. The solution was cooled and diluted with 85 mL of MeOH. A 40% aqueous solution of NaOH (7.5 mL, 75 mmol) was added dropwise to the MeOH solution which was stirred at room temperature for 2.5 h. The excess base was neutralized by the addition of 20 mL of 3 N HCl and the solution was concentrated in vacuo. The residue was extracted with ether. The ether solution was washed with water and dried, an aliquoit was removed for HPLC analysis, and the remainder of the ether solution was concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 50 g; eluents, CH_2Cl_2 and then ether CH_2Cl_2 (1:4 v/v)) to give in the first product band 2.5 g of an oil. The oil was treated with 15 mL of a 1.4 M MeOH solution of HCl and diluted with ether. The resulting precipitate was collected by filtration to give 1.6 g (41%, mp 231–233 °C dec) of the hydrochloride salt of **14b** as an off-white solid. Recrystallization from CH_2Cl_2/ether gave **14b** as colorless crystals: mp 232–234 °C; IR (KBr) 2500, 2280, 2135 (NH), 1640 (C=N) cm^{-1}, NMR (Me_2SO-d_6) δ 3.80 (br s, 2,

C_3H), 6.82 (t, J = 7 Hz, 1, C_4H), 7.1–8.0 (m, 7, Ar H), 9.19 (s, 1, NH). Anal. Calcd for $C_{16}H_{11}BrCl_2FN$: C, 49.67, H, 2.86; N, 3.62. Found: C, 49.62; H, 2.86; N, 3.63.

The second product band gave 1.45 g of an oil. The oil was treated with 10 mL of a 1 N MeOH solution of methanesulfonic acid and diluted with ether. The resulting precipitate was collected by filtration to give 1.7 g (43%) of the methanesulfonate salt of **16b** as colorless prisms. Recrystallization from MeOH/ether gave the methanesulfonate salt of **16b** as colorless prisms: mp 155–156 °C; IR (KBr) 2540, 2175 (NH), 1623 (C=N) cm^{-1}; NMR (Me_2SO-d_6) δ 2.55 (s, 3, CH_3), 3.46 (s, 3, CH_3), 4.31 (dd, J = 2, 4 Hz, 1, C_3H), 6.22 (dd, J = 4, 10 Hz, 1, C_4H), 6.90 (dd, J = 2, 10 Hz, 1, C_5H), 7.1–7.7 (m, 7, Ar H), 10.01 (s, 1, NH). Anal. Calcd for $C_{19}H_{17}ClFNO_4S$: C, 54.34; H, 4.31; N, 3.52. Found: C, 54.45; H, 4.30; N, 3.23.

5-Bromo-8-chloro-1-(2-fluorophenyl)-3*H*-2-benzazepine Hydrochloride (14b) and 8-Chloro-1-(2-fluorophenyl)-3-(1,1-dimethylethoxy)-3*H*-2-benzazepine (15b). Powdered KOH (1.1 g, 20 mmol) was added to a well-stirred solution of 4.3 g (10 mmol) of **13b** and 10 mL of THF in 50 mL of *tert*-butyl alcohol in a water bath at room temperature. The mixture was stirred for 75 min, and the excess KOH was neutralized with the addition of 4.0 mL of 3 N aqueous HCl and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 50 g, eluent, CH_2Cl_2) to give an oil. The oil was diluted with 20 mL of a 1.4 M MeOH solution of HCl followed by ether. The resulting precipitate was collected by filtration to give 2.7 g (70%) of the hydrochloride salt of **14b** as a colorless solid which was identical in every respect by mp, mmp, and NMR to an authentic sample. The second product band gave 90 mg of an oil which by TLC (SiO_2, EtOAc/petroleum ether (1:3 v/v)) was a mixture of two components. The oil was rechromatographed (SiO_2, 10 g; eluent, EtOAc/petroleum ether (1:3 v/v)) to give in the first product band 40 mg (1%) of **15b** as a colorless oil which crystallized upon standing: mp 111–112 °C; NMR ($CDCl_3$) δ 1.28 (s, 9, $3CH_3$), 4.56 (dd, J = 1, 4 Hz, 1, C_3H), 6.23 (dd, J = 4, 10 Hz, 1, C_4H); mass spectrum, m/e 344 (M^+).

The second product band gave 10 mg (1%) of **6b** as a colorless oil which was spectroscopically identical by IR, MS, and NMR with an authentic sample.

5-Bromo-8-chloro-1-phenyl-3*H*-2-benzazepine Hydrochloride (14c) and 8-Chloro-3-methoxy-1-phenyl-3*H*-2-benzazepine Methanesulfonate Salt (16c). Compounds **14c** and **16c** were prepared in the same manner as the preparation of **14b** and **16b** to give **14c** as colorless prisms: mp 230–235 °C dec; IR (KBr) 2380, 2175, 2130 (NH), 1630 (C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{12}BrCl_2N$: C, 52.06; H, 3.28; N, 3.80. Found: C, 52.06; H, 3.05; N, 3.61.

Compound **16c** was obtained as gray prisms: mp 139–140 °C; IR ($CHCl_3$) 2460–2700, 1980 (NH), 1625 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.75 (s, 3, CH_3), 3.55 (s, 3, OCH_3), 5.40 (d, J = 5 Hz, 1, C_3H), 6.49 (dd, J = 5 Hz, 1, C_4H), 7.03 (d, J = 11 Hz, 1, C_5H), 7.4–7.8 (m, 18, Ar H), and 12.86 (br s, 1, NH). Anal. Calcd for $C_{17}H_{14}ClNO{\cdot}CH_4SO_3$: C, 56.91; H, 4.78; N, 3.69. Found: C, 56.60; H, 4.79; N, 3.66.

5-Bromo-8-chloro-1-phenyl-3*H*-2-benzazepine Hydrochloride (14c). Compound **14c** was prepared in the same manner as the preparation of **14b** and **15b** to give **14c** which was identical in every respect with an authentic sample. Compound **15c** was neither isolated nor observed in this reaction.

5-Azido-8-chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine (17) and 3-Azido-8-chloro-1-(2-chlorophenyl)-3*H*-2-benzazepine (18). A mixture of 3.0 g (6.7 mmol) of **13a** and 4.0 g (61 mmol) of sodium azide in 20 mL of dimethyl sulfoxide was stirred at room temperature for 3 h. The mixture was diluted with water and extracted with ether. The ether solution was washed with water, dried, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, 100 g; eluent, CH_2Cl_2) to give in the first product band 0.2 g (9%) of **18** as gray prisms: mp 97–99 °C; IR ($CHCl_3$) 2325 (N_3), 1612 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 4.59 (dd, J = 2, 5 Hz, 1, C_3H), 6.11 (dd, J = 5, 10 Hz, 1, C4H), 6.77 (dd, J = 2, 10 Hz, 1, C5*H*), 7.1–7.7 (m, 7, Ar H); mass spectrum, m/e 328 (M^+). Anal. Calcd for $C_{16}H_{10}Cl_2N_4$: C, 58.38; H, 3.06; N, 17.02. Found: C, 58.27; H, 3.08; N, 16.91.

The second product band gave 1.3 g (59%) of **17** as pale yellow needles: mp 103–104 °C; IR ($CHCl_3$) 2325 (N_3), 1615 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 3.81 (br d, J = 7 Hz, 2, C_3H), 6.05 (t, J = 7 Hz, 1, C4*H*), 7.1–7.6 (m, 6, Ar H), 7.69 (d, J = 8 Hz, 1, Ar H); mass spectrum m/e 328 (M^+). Anal. Calcd for $C_{16}H_{10}Cl_2N_4$: C, 58.38; H, 3.06; N, 17.02. Found: C, 58.52; H, 3.09; N, 17.07.

8-Chloro-1-phenyl-3*H*-2-benzazepine-5-carboxylic Acid Butyl Ester (19c) and 8-Chloro-1-phenyl-5*H*-2-benzazepine-5-carboxylic Acid Butyl Ester (20c). The preparation of **19c** and **20c** was conducted in the same manner as the preparation of **21c** and **22c** with the exception that 1-butanol was used as cosolvent. Purification of the reaction mixture by column chromatography gave in the first product band 0.5 g (14%) of **20c** as a pale yellow oil: IR ($CHCl_3$) 1735 (ester) cm^{-1}; NMR ($CHCl_3$) δ 0.86 (m, 3, CH_3) 1.4 (m, 4, $2CH_2$), 3.6–4.4 (m 3, C_5HCH_2, 5.7 (br s, 1, C_4H), 6.9–7.9 (m, 9, Ar H C_3H); mass spectrum, m/e 353 (M^+).

The second product band gave 1.1 g (30%) of **19c** as a yellow oil: IR ($CHCl_3$) 1712 (ester) cm^{-1}; NMR ($CDCl_3$) δ 0.88 (t, 3, CH_3), 1.5 (m, 4, $2CH_2$), 4.2 (t, 2, CH_2), 6.7–7.9 (m, 9, Ar H C_4H); mass spectrum, m/e 353 (M^+).

8-Chloro-1-phenyl-3*H*-2-benzazepine-5-carboxylic Acid Methyl Ester Hydrochloride (21c) and 8-Chloro-1-phenyl-5*H*-2-benzazepine-5-carboxylic Acid Methyl Ester (22c). A mixture of 3.4 g (10 mmol) of **14c**, 150 mg (0.2 mmol) of dibromobis(triphenylphosphine)palladium(II), 80 mg (0.4 mmol) of cuprous iodide, 2.6 mL (2.0 g, 10.8 mmol) of tri-*n*-butylamine, and 2.0 mL of MeOH was degassed with argon in a 200-mL glass pressure bottle equipped with two valves and a pressure gauge. The bottle was charged with 40 psi of carbon monoxide and heated at 100 °C until the uptake of carbon monoxide ceased (3 h). The mixture was cooled and diluted with ether. The ether solution was washed with 1 N aqueous HCl, dilute $NaHCO_3$, and water, dried, and concentrated in vacuo to dryness. The residue was purified by column chromatography (SiO_2, 200 g; eluent, ether-/CH_2Cl_2 (1:19 v/v)) to give in the first product band 1.3 g (41%, mp 100–102 °C) of **22c** as a yellow solid. Recrystallization from ether gave **22c** as pale yellow crystals: mp 103–105 °C; IR ($CHCl_3$) 1741 (ester) cm^{-1}; NMR ($CDCl_3$) δ 3.88 (br s, 3, CH_3), 5.7 (br s, 1, C_5H), 6.95 (d, J = 7 Hz, 1, C_4H), 7.0–7.9 (m, 9, Ar H C_3H); mass spectrum, m/e 311 (M^+). Anal. Calcd for $C_{18}H_{20}NO_2Cl$: C, 69.34; H, 4.52; N, 4.49. Found: C, 69.60; H, 4.53; N, 4.55.

The second product band gave 1.2 g (38%) of **21c** as a colorless oil. The oil was dissolved in 1.4 M methanolic HCl and diluted with ether to give the hydrochloride salt of **21c** as off-white needles: mp 197–199 °C; IR (KBr) 3430 (OH), 2400 (NH^+), 1708 (ester) cm^{-1}; NMR (Me_2SO-d_6) δ 3.82 (s, 3, CH_3), 3.8 (br s, 1) and 4.4 (br s, 1) (AB system, C_3H), 7.39 (t, J = 7 Hz, 1, C_4H), 7.2 (br s, 1, NH^+), 7.39 (t, J = 7 Hz, 1, C_4H), 7.46 (d, J = 2 Hz, 1, Ar H) 7.5–8.1 (m, 7, Ar H). Anal. Calcd for $C_{18}H_{15}Cl_2NO_2$: C, 62.09; H, 4.34; N, 4.02. Found: C, 62.37; H, 4.04; N, 4.29.

8-Chloro-1-phenyl-3*H*-2-benzazepine-5-carboxylic Acid 1,1-Dimethylethyl Ester (23c) and 8-Chloro-1-phenyl-5*H*-2-benzazepine-5-carboxylic Acid 1,1-Dimethylethyl Ester (24c). The preparation of **23c** and **24c** was conducted in the same manner as the preparation of **21c** and **22c** with the exception that *tert*-butylalcohol (5 g) was used as cosolvent. Purification of the reaction mixture by column chromatography gave in the first product band 0.5 g (14%) of **24c** as pale yellow crystals: mp 141–143 °C; IR ($CHCl_3$) 1728 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.2 (br s) and 1.55 (br s) (9, $3CH_3$), 3.7 (br s) and 4.15 (br s) (1, C_5H), 5.66 (br s, 1 C_4H), 6.92 (d, J = 7 Hz, 1, C_4H), 7.1–7.9 (m, 8, Ar H); mass spectrum, m/e 353 (M^+). Anal. Calcd for $C_{21}H_{20}ClNO_2$: C, 71.29; H, 5.69; N, 3.95. Found: C, 71.36; H, 5.61; N, 3.98.

The second product band gave 2.05 g (57%) of **23c** as yellow crystals: mp 120–122 °C; IR ($CHCl_3$) 1705 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.43 (s, 9, $3CH_3$), 3.08 (br s, 1) and 4.46 (br s, 1) (AB system, C_3H), 7.2–7.6 (m, 8, Ar H, C_4H), 7.79 (d, J = 8 Hz, 1, Ar H); mass spectrum, m/e 353 (M^+). Anal. Calcd for $C_{21}H_{20}ClNO_2$: C, 71.28; H, 5.69; N, 3.95. Found: C, 71.02; H, 5.79; N, 3.98.

9-Chloro-3-methyl-7-(2-chlorophenyl)-5*H*-pyrimido[4,5-*d*][2]benzazepin-1(2*H*)-one (25a). The preparation of **25a** was conducted in the same manner as the preparation of **25c** starting from **14a** to give **25a** in 23% yield as colorless prisms: mp 277–279 °C; IR (KBr) 1664 (C=O), 1600 (C=N) cm^{-1}; NMR ($CDCl_3$, Me_2SO-d_6) 3.0 (s, 3, CH_3), 3.73 (d, J = 10 Hz, 1) and 4.84 (d, J = 10 Hz, 1) (AB system, C_5H), 7.04 (d, J = 2 Hz, Ar H), 7.2–7.6 (m, 5, Ar H), 8.19 (d, J = 9 Hz, 1 Ar H), 12.68 (br s, 1, NH); mass

spectrum, m/e 369 (M^+). Anal. Calcd for $C_{19}H_{13}Cl_2N_3O$: C, 61.64; H, 3.54; N, 11.35. Found: C, 61.78; H, 3.69; N, 11.36.

9-Chloro-3-methyl-7-(2-fluorophenyl)-5*H*-pyrimido[4,5-*d*][2]benzazepin-1(2*H*)-one (25b). The preparation of **25b** was conducted in the same manner as the preparation of **25c** starting from **14b** to give **25b** in 24% yield as yellow prisms: 262–264 °C; IR (KBr) 2708 (NH), 1667 (C=O) cm^{-1}; NMR (Me_2SO-d_6) 2.43 (s, 3, CH_3), 3.61 (d, J = 10 Hz, 1) and 4.76 (d, J = 10 Hz, 1) (AB system, C_5H), 7.0–7.7 (m, 6, Ar H), 8.20 (d, J = 8 Hz, 1, Ar H), 11.01 (s, 1, NH); mass spectrum, m/e 353 (M^+). Anal. Calcd for $C_{19}H_{13}ClFN_3O$: C, 64.50; H, 3.70; N, 11.88. Found: C, 64.22; H, 3.90; N, 11.73.

9-Chloro-3-methyl-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benzazepin-1(2*H*)-one (25c). A mixture of 9.0 g (27 mmol) of **14c**, 0.2 g (0.25 mmol) of dibromobis(triphenylphosphine)palladium(II), 7.0 mL (5.4 g, 29 mmol) of tri-*n*-butylamine, and 4.8 mL of 1-butanol was degassed in a 200-mL glass pressure bottle equipped with two pressure valves and a pressure gauge. The bottle was charged with 40 psi of carbon monoxide and heated to 100 °C until the uptake of carbon monoxide ceased (18 h). The mixture was cooled and diluted with ether. The ether solution was washed with 1 N aqueous HCl, dilute $NaHCO_3$ and water, dried, and concentrated in vacuo to dryness to give 12.6 g of an amber oil.

The 12.6 g of butyl esters, 4.0 g (42 mmol) of acetamidine hydrochloride, and 10.0 mL (4.0 M, 40 mmol) of methanolic sodium methoxide in 200 mL of ethanol was refluxed for 6 h. The mixture was cooled, diluted with water, and concentrated in vacuo until the ethanol was removed. The residue was suspended in a mixture of ether and water and the precipitate was collected by filtration. The precipitate was washed with water, ether, and petroleum ether to give 5.1 g of a yellow solid.

The 5.1 g of the yellow solid and 10 g of MnO_2 in 470 mL of THF was refluxed for 4 h. The mixture was filtered over Celite and the filtrate was concentrated to dryness. The residue was triturated with ether/petroleum ether to give 3.6 g (40%, mp 250–256 °C) of **25c** as a yellow solid. Recrystallization from ether/CH_2Cl_2 gave **25c** as colorless prisms: mp 263–264 °C; IR (KBr) 3430 (OH), 1653 (C=O), 1600 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.49 (s, 3, CH_3), 3.78 (d, J = 9 Hz, 1) and 4.95 (d, J = 9 Hz, 1) (AB system, C_5H), 7.2–7.6 (m, 8, Ar H, NH), 8.17 (d, J = 8 Hz, 1 Ar H); mass spectrum, m/e 335 (M^+). Anal. Calcd for $C_{19}H_{14}ClN_3O$: C, 67.96; H, 4.20; N, 12.51. Found: C, 67.72; H, 4.26; N, 12.23.

3-Amino-9-chloro-7-(2-fluorophenyl)-5*H*-pyrimido[4,5-*d*][2]benzazepin-1(2*H*)-one (26b). The preparation of **26b** was conducted in the same manner as the preparation of **25c** starting from **14b** and guanidinecarbonate to give **26b** in 30% yield as off-white prisms: mp 331–332 °C; IR (KBr) 3245, 3120 (OH, NH) 1658, 1650 (C=O), 1608 (C<<dbN) cm^{-1}; NMR (Me_2SO-d_6) δ 3.57 (d, J 10 Hz, 1) and 4.59 (d, J = 10 Hz, 1) (AB system), C_5H), 6.77 (br s, 2, NH_2), 7.0–7.7 (m, 6, Ar H), 8.09 (d, J = 8 Hz, 1, Ar H), 11.01 (br s, 1, OH); mass spectrum, m/e 354 (M^+). Anal. Calcd for $C_{18}H_{12}ClFN_4O$: C, 60.94; H, 3.41; N, 15.79. Found: C, 60.79; H, 3.07; N, 15.37.

1,9-Dichloro-3-methyl-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benzazepine (27). A solution of 3.5 g (10.4 mmol) of **25c** and 22 mL of phosphorous oxychloride in 100 mL of CH_2Cl_2 was stirred at room temperature for 18 h. The reaction mixture was concentrated in vacuo to a solid residue. The residue was partitioned between ice cold aqueous $NaHCO_3$ and CH_2Cl_2. The CH_2Cl_2 solution was dried and concentrated in vacuo to a yellow solid. Purification by column chromatography (SiO_2, 40 g; eluents CH_2Cl_2/ether (9:1 v/v)) gave 2.3 g (62%, mp 190–192 °C) of **27** as a pale yellow solid. Recrystallization from ether/petroleum ether gave **27** as colorless prisms: mp 191–193 °C; IR ($CHCl_3$) 1608 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.70 (s, 3, CH_3), 3.99 (d, J = 10 Hz, 1) and 5.10 (d, J = 10 Hz, 1) (AB system, C_5H), 7.2–7.8 (m, 7, Ar H), 7.92 (d, J = 10 Hz, 1, Ar H); mass spectrum, m/e 353 (M^+). Anal. Calcd for $C_{19}H_{13}Cl_2N_3$: C, 64.42; H, 3.70; N, 11.86. Found: C, 64.48; H, 3.48; N, 11.61.

9-Chloro-1-methoxy-3-methyl-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benzazepine (28). A solution of 1.0 g (2.8 mmol) of **27** and 1.0 mL of a 4.2 M MeOH solution of sodium methoxide in 20 mL of MeOH/THF (1:1 v/v) was stirred at room temperature for 1 h. The solvent was removed in vacuo and the residue was triturated with water to give 0.9 g (90%) of **28** as an off-white solid. Recrystallization from ether/petroleum ether gave 0.5 g of **28** as colorless prisms: mp 185–187 °C; IR (KBr) 1608 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.6 (s, 3, CH_3), 3.88 (d, J = 10 Hz, 1) and 5.03 (d, J = 10 Hz, 1) (AB system, C_5H), 4.0 (s, 3, OCH_3), 7.2–7.6 (m, 7, Ar H), 7.88 (d, J = 8 Hz, 1, Ar H); mass spectrum, m/e 349 (M^+). Anal. Calcd for $C_{20}H_{11}N_3O$: C, 68.67; H, 4.61; N, 12.01. Found: C, 68.66; C, 4.54; N, 12.06.

9-Chloro-3-methyl-1-(methylthio)-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benzazepine (29). Compound **27** (1.0 g, 2.8 mmol) was added in one portion to a solution of 150 mg (3.1 mmol) of a 50% mineral oil suspension of sodium hydride and an excess of methyl mercaptan (>3.1 mmol) in 25 mL of DMF. The mixture was stirred at room temperature for 30 min and diluted with water. The resulting precipitate was collected by filtration to give 0.9 g (90%) of **29** as a yellow solid. Recrystallizatioyn from ether/CH_2Cl_2 gave **29** as pale yellow prisms: mp 181–183 °C; IR (KBr) 1604 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.51 (s, 3, CH_3), 3.87 (d, J = 10 Hz, 1), 5.02 (d, J = 10 Hz, 1) (AB system, C_5H), 7.25–7.65 (m, 7, Ar H) 8.0 (d, J = 8 Hz, 1, Ar H); mass spectrum, m/e 365 (M^+). Anal. Calcd for $C_{20}H_{18}ClN_3S$: C, 65.65; H, 4.40; N, 11.48. Found: C, 65.47; H, 4.51; N, 11.43.

***N*-(9-Chloro-3-methyl-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benzazepin-1-yl)-*N*,*N*-dimethyl-1,3-propanediamine $^1/_3$ Hydrate (30).** A solution of 1.0 g (2.8 mmol) of **27** and 1 mL of (dimethylamino)propylamine in 25 mL of DMF was heated to 65 °C for 16 h. The mixture was poured into ice water and the resulting precipitate was collected by filtration to give 0.8 g (78%) of **30** as a tan solid. Recrystallization from ether/petroleum ether gave **30** as colorless needles: mp 124–127 °C; IR (KBr) 3460 (NH), 1605 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 1.69 (m, 2, CH_2), 2.04 (s, 6, CH_3), 2.40 (m, 2, CH_2), 2.48 (s, 3, CH_3), 3.53 (d, J = 6 Hz, 2, CH_2), 3.75 (d, J = 10 Hz, 1) and 4.87 (d, J = 10 Hz, 1) (AB system, C_5H), 7.2–7.9 (m, 9, Ar H, NH); mass spectrum m/e 419 (M^+). Anal. Calcd for $C_{24}H_{26}ClN_5 \cdot {}^1/_3H_2O$: C, 67.61; H, 6.31; N, 16.44. Found: C, 67.71; H, 6.49; N, 16.71.

The hydrochloride salt of **30** was prepared by the addition of 1 molar equiv of a 1.4 M methanolic solution of HCl to an ether solution of **30** and was isolated by filtration. Recrystallization of the hydrochloride salt of **30** from MeOH/ether gave the salt as off-white prisms: mp 190–194 °C; IR (KBr) 3335 (NH), 1610 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.14 (m, 2, CH_2), 2.48 (s, 3, CH_3), 2.77 (s, 6, CH_3), 3.05 (m, 2, CH_2), 3.65 (m, 2, CH_2), 3.77 (d, J = 11 Hz, 1) and 4.89 (d, J = 11 Hz, 1) (AB system, C_5H), 6.71 (t, J = 6 Hz, 1, NH), 7.3–7.7 (m, 7, Ar H) 7.77 (d, J = 8 Hz, 1, Ar H). Anal. Calcd for $C_{24}H_{28}Cl_2N_5 \cdot H_2O$: C, 60.75; H, 6.16; N, 14.76. Found: C, 60.57; H, 5.92; N, 14.79.

9-Chloro-1,3-dimethyl-7-phenyl-5*H*-pyrimido[4,5-*d*][2]benazepine 0.25 Etherate (31). Dropwise 13.2 mL (18.5 mmol) of a 1.4 M ether solution of methylithium was added to a suspension of 1.7 g (8.9 mmol) of cuprous iodide in 50 mL of ether which was cooled to 0 °C. A solution of 0.8 g (2.2 mmol) of **27** in 30 mL of ether was added dropwise to the solution of lithium dimethylcuprate which was cooled to −25 °C. The mixture was stirred at −25 °C for 1 h, warmed to room termperature, diluted with water, and saturated with hydrogen sulfide. The resulting precipitate was removed by filtration over Celite and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (SiO_2, 10 g; eluent, ether/CH_2Cl_2 (1:4 v/v)) gave after crystallization from ether/petroleum ether 0.4 g (53%) of **31** as off-white needles: mp 121–124 °C; IR (KBr) 1605 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 1.2 (t, J = 7 Hz, 1.5 CH_3 of ether), 2.61 (s, 3, CH_3), 2.70 (s, 3, CH_3), 3.47 (d, J = 7 Hz, 1, CH_2 of ether), 3.99 (d, J = 10 Hz, 1) and 5.06 (d, J = 10 Hz, 1) (AB system, C_5H), 7.3–7.7 (m, 8, Ar H); mass spectrum, m/e 333 (M^+). Anal. Calcd for $C_{20}H_{16}ClN_3 \cdot 0.25C_4H_{10}O$: C, 71.57; H, 5.26; N, 11.92. Found: C, 71.78; H, 5.22; H, 11.92.

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3-methoxy-3*H*-2-benzazepine (33) from 16a. A solution of 1.0 g (3.1 mmol) of **16a** and two spatulas full of Raney nickel[28] in 50 mL of THF was hydrogenated at room temperature and atmospheric pressure for 1 h. The nickel was removed by filtration and the filtrate was concentrated in vacuo. The residue crystallized from ether/petroleum ether to give 0.2 g (20%) of **33** as a colorless solid. Recrystallization from ether gave **33** as colorless prisms: mp 108–110 °C; IR ($CHCl_3$) 1614 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.3–3.0 (m, 4, 2 CH_2), 4.22 (dd, J = 7, 10 Hz, 1, C_3H), 6.90 (d, J = 2 Hz, 1,

Ar H), 7.1–7.7 (m, 6, Ar H); mass spectrum, *m/e* 321 (M^+). Anal. Calcd for $C_{17}H_{15}Cl_2NO$: C, 63.76; H, 4.72; N, 4.37. Found: C, 63.45; H, 4.63; N, 4.37.

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3-methoxy-3*H*-2-benzazepine (33) and (2-Chlorophenyl)[4-chloro-2-(3,3-dimethoxypropanyl)phenyl]methanone Imine (34) from 36. A solution of 1.0 g (3 mmol) of **36** and 50 mL of 1.4 M MeOH solution of HCl was stirred at room temperature for 4 h. The solution was poured into 200 mL of saturated aqueous $NaHCO_3$ and extracted with ether. The ether solution was washed with water, dried, and concentrated in vacuo. Purification of the residue by column chromatography (SiO_2, 100 g; eluent EtOAc/petroleum ether (1:3 v/v)) gave in the first product band 0.4 g (44%) of **33** as colorless crystals: mp 109–111 °C, identical by mmp and NMR with **33** obtained from **16a**.

The second product band gave 0.4 g (38%) of **34** as a pale yellow oil: NMR ($CDCl_3$) δ 1.83 (m, 2, CH_2), 2.70 (m, 2, CH_2), 3.23 (s, 6, 2 CH_3), 4.23 (t, J = 6 Hz, 1, CH), 7.2–7.6 (m, 6, Ar H); mass spectrum, *m/e* 351 (M^+).

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3*H*-2-benzazepine 2-Oxide (35). A solution of 13 g (45 mmol) of **8a** and 10.9 g (54 mmol) of *m*-chloroperoxybenzoic acid in 130 mL of CH_2Cl_2 was stirred for 30 min. The solution was washed with aqueous Na_2CO_3 and H_2O, dried, and concentrated in vacuo to dryness. The resulting precipitate was triturated with ether to give 13.2 g (96%) of **35** as a colorless solid. Recrystallization from EtOAc gave **35** as colorless crystals: mp 187–189 °C; NMR ($CDCl_3$) δ 2.52 (quintet, J = 7 Hz, 2, C_4H), 3.01 (t, J = 7 Hz, 2, C_5H), 4.11 (t, J = 7 Hz, 2, C_3H), 6.88 (br s, 1, Ar H), 7.1–7.6 (m, 7, Ar H); mass spectrum, *m/e* 305 (M^+). Anal. Calcd for $C_{16}H_{13}Cl_2NO$: C, 62.75; H, 4.28; N, 4.57. Found: C, 62.80; H, 4.31; N, 4.60.

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3*H*-2-benzazepin-3-ol Acetate (36). A mixture of 13 g (42 mmol) of **35** and 150 mL of acetic anhydride was refluxed for 4 h. The acetic anhydride was removed in vacuo. The residue was poured over ice, basified with $NaHCO_3$, and extracted with ether. The ether solution was washed with water, dried, and concentrated in vacuo. The residue was triturated with ether to give 11.2 g (77%) of **36** as a tan solid. Recrystallization from ether/petroleum ether (charcoal) gave **36** as colorless prisms: mp 118–120 °C; IR (KBr) 1738 (C=O), 1619 (C=N) cm^{-1}; NMR ($CDCl_3$) δ 2.12 (s, 3, CH_3), 2.4–3.1 (m, 4, $2CH_2$), 5.65 (t, J = 8 Hz, 1, C_3H), 6.91 (d, J = 2 Hz, 1, Ar H), 7.2–7.7 (m, 6, Ar H); mass spectrum, *m/e* 305 ($M^+ - CH_2CO$). Anal. Calcd for $C_{19}H_{15}Cl_2NO_2$: C, 62.09; H, 4.34; N, 4.02. Found: C, 61.89; H, 4.32; N, 3.97.

8-Chloro-1-(2-chlorophenyl)-4,5-dihydro-3*H*-2-benzazepin-5-ol (37). Lithium aluminum hydride (150 mg, 4 mmol) was added to a solution of 0.5 g (1.6 mmol) of **3a**[5] in 20 mL of THF which was cooled to −78 °C. The mixture was allowed to warm to room temperature and stirred for 30 min. The excess lithium aluminum hydride was discharged by sequential addition of 1 mL of water, 1 mL of 3 N aqueous NaOH, and 3 mL of water. The precipitate was removed by filtration and the filtrate was concentrated in vacuo to give 0.4 g (80%) of **37** as a colorless solid. Recrystallizatiyon from CH_2Cl/ether gave **37** as colorless prisms: mp 205–206 °C; IR (KBr) 3160 (OH), 1623 (C=N) cm^{-1}; NMR ($CDCl_3$, Me_2So-d_6) δ 2.04 (m, 2, C_4H), 2.9–3.1 (m, 1, C_3H), 3.7–4.0 (m, 1, C_3H), 4.88 (m, 1, C_5H), 5.23 (d, J = 4 Hz, 1, OH), 6.82 (d, J = 2 Hz, 1, Ar H), 7.2–7.8 (m, 6, Ar H): mass spectrum, *m/e* 305 (M^+). Anal. Calcd for $C_{16}H_{13}Cl_2NO$: C, 62.76; H, 4.28; N, 4.57. Found: C, 62.54; H, 3.97; N, 4.77.

8-Chloro-1-(2-chlorophenyl)-5-methoxy-4,5-dihydro-3*H*-2-benzazepine Methanesulfonate Salt (38). A solution of 0.8 mL (2.4 M, 1.9 mmol) of *n*-butyllithium in hexane was added to a solution of 0.5 g (1.6 mmol) of **37** in 20 mL of THF which was cooled to −78 °C. The solution was treated with 0.5 mL (8 mmol) of methyl iodide. The mixture was allowed to warm to room temperature and stirred overnight. The solution was diluted with CH_2Cl_2, washed with water, dried, and concentrated in vacuo. Purification of the resiude by column chromatography (SiO_2; eluent, CH_2Cl_2/ether (9:1 v/v)) gave 0.1 g of a colorless oil. The oil was dissolved in 0.3 mL of a 1.0 M MeOH solution of methanesulfonic acid and diluted with ether. The resulting precipitate was collected by filtration to give 120 mg (18%) of **38** as colorless prisms: mp 185–187 °C; NMR ($CDCl_3$) δ 2.60 (m, 1, C_4H), 2.72 (s, 3, CH_3), 3.15 (m, 1, C_4H), 3.37 (s, 3, CH_3), 3.67 (m, 1, C_3H), 4.09 (7, 1, C_3H), 4.51 (t, J = 7 Hz, 1, C_5H), 7.11 (br s, 1, Ar H), 7.4–8.0 (m, 6, Ar H); mass spectrum, *m/e* 321 ($M^+ - CH_3SO_3H$). Anal. Calcd for $C_{19}H_{21}Cl_2NO_4S$: C, 51.93; H, 4.60; N, 3.36. Found: C, 52.08; H, 4.70; N, 3.61.

4-Bromo-8-chloro-1-(2-chlorophenyl)-3,4-dihydro-5*H*-2-benzazepin-5-one Hydrobromide (42). A 5% (v/v) CH_2Cl_2 solution of bromine (15 mL, 14 mmol) was added dropwise to a solution of 4.7 g (10 mmol) of the hydrobromide salt of **3a**[5] in 200 mL of CH_2Cl_2. The mixture was stirred for 30 min and the resulting precipitate was collected by filtration to give 5.4 g (95%) of **42** as a colorless solid. Recrystallization from MeOH/ether gave **42** as colorless crystals: mp 175–190 °C; IR (KBr) 1695, 1653 (C=O) cm^{-1}; NMR (Me_2SO-d_6) δ 4.12 (dd, J = 8, 12 Hz, 1) and 4.52 (dd, J = 3, 12 Hz, 1) (AB system, C_3H), 5.32 (dd, J = 3, 8 Hz, 1, C_4H), 6.4 (s, 1, NH), 7.01 (s, 1, Ar H), 7.2–7.9 (m, 6, Ar H). Anal. Calcd for $C_{16}H_{11}Br_2Cl_2NO$: C, 41.42; H, 2.39; N, 3.02. Found: C, 41.28; H, 2.47; N, 2.96.

8-Chloro-1-(2-chlorophenyl)-5*H*-2-benzazepin-5-one (43). A solution of 4.0 mL (29 mmol) of triethylamine in 10 mL of CH_2Cl_2 was added to a suspension of 4.0 g (8.6 mmol) of **42** in 50 mL of CH_2Cl_2. The mixture was stirred at room temperature for 3 h and diluted with 100 mL of ether. The ether solution was washed with water, 2% aqueous HOAc, and water, dried, and concentrated in vacuo to dryness. The residue was triturated with ether/petroleum ether (1:1 v/v) to give 2.4 g (93%, mp 103–104 °C) of **43** as a yellow solid. Recrystallization from ether/petroleum ether gave **43** as yellow crystals: mp 105–106 °C; IR ($CHCl_3$) 1645 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 6.29 (d, J = 9 Hz, 1 C_4H) 7.3–7.9 (m, 7, Ar H), 8.09 (d, J = 9 Hz, 1, C_3H); mass spectrum, *m/e* 301 (M^+). Anal. Calcd for $C_{16}H_9Cl_2NO$: C, 63.60; H, 3.00; N, 4.64. Found: C, 63.55; H, 3.16; N, 4.61.

8-Chloro-1-(2-chlorophenyl)-5*H*-2-benzazepin-5-one (43) from 3a. A 5% solution (v/v) of bromine in CH_2Cl_2 (42 mL, 38 mmol) was added dropwise to a solution of 13.1 g (28 mmol) of the hydrobromide salt of **3a**[5] in 400 mL of CH_2Cl_2. The mixture was stirred for 10 min followed by the dropwise addition of 17 mL (120 mmol) of triethylamine in 80 mL of CH_2Cl_2. The resulting solution was stirred for 2 h. The CH_2Cl_2 solution was successively washed with water, 5% (v/v) aqueous HOAc, water, and saturated aqueous $NaHCO_3$, dried, and concentrated in vacuo to dryness. The residue was purified by column chromatography (SiO_2, 150 g; eluent, CH_2Cl_2/petroleum ether (1:1 v/v)) to give 7.5 g (89%) of **43** as a yellow solid which was identical in every respect with an authentic sample.

8-Chloro-1-(2-chlorophenyl)-5*H*-2-benzazepin-5-ol (44) and 8-Chloro-1-(2-chlorophenyl)-1,2-dihydro-5*H*-2-benzazepin-5-one (45). A solution of 7.5 g (25 mmol) of **43** in 50 mL of THF was added dropwise to a solution of 2.0 g (52 mmol) of lithium aluminum hydride in 100 mL of THF which was cooled to −78 °C. The mixture was stirred for 30 min and the excess lithium aluminum hydride was discharged by the successive addition of 5 mL of water and 1 mL of 40% aqueous NaOH. The THF solution was washed with 1 N aqueous HCl and water, dried, and concentrated in vacuo to dryness. Trituration of the residue with ether gave 1.2 g of pure **45**. The filtrate was purified by column chromatography (SiO_2, 240 g; eluents ethyl acetate/petroleum ether (1:2 v/v) and then EtOAc) gave in the first product band 4.0 g (53%) of **44** as a colorless solid. Recrystallization from ether/petroleum ether gave **44** as colorless crystals: mp 151–152 °C; IR (KBr) 3200 (OH) cm^{-1}; NMR ($CDCl_3$) δ 4.87 (m, 1, C_5H), 5.48 (dd, J = 4, 8 Hz, 1, C_4H), 5.73 (d, J = 4 Hz, 1, OH), 6.78 (dd, J = 2, 8 Hz, 1, C_3H), 6.93 (d, J = 2 Hz, 1, Ar H), 7.3–7.8 (m, 6, Ar H); mass spectrum, *m/e* 303 (M^+). Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.19; H, 3.65; N, 4.60. Found: C, 63.10; H, 3.76; N, 4.72.

The second product band gave 0.9 g (28% combined yield) of **45** as a colorless solid. Recrystallization from CH_2Cl_2/ether gave **45** as colorless crystals: mp 233–234 °C; IR (KBr) 3260 (NH), 1595 1535 (C=O), 1535 (C=C) cm^{-1}; NMR (Me_2SO-d_6) δ 5.28 (dd, J = 1, 8 Hz, 1, C_4H), 5.78 (d, J = 4 Hz, 1, C_1H), 6.57 (d, J = 2 Hz, 1, Ar H), 7.11 (dd, J = 6, 8 Hz, 1, C_3H), 7.2–7.9 (m, 6, Ar H), 8.28 (br s, 1, NH); mass spectrum, *m/e* 303 (M^+). Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.19; H, 3.65; N, 4.60. Found: C, 63.26; H, 3.78; N, 4.63.

8-Chloro-1-(2-chlorophenyl)-3-methoxy-3*H*-2-benzazepine (16a) from 44. Method A. A mixture of 0.3 g (1 mmol) of **44**

and 0.2 mL of triethylamine in 20 mL of CH_2Cl_2 was refluxed until solution was complete. The solution was cooled to −5 °C and 1 mL (1.3 mmol) of a 10% (v/v) CH_2Cl_2 solution of methanesulfonyl chloride was added dropwise. The solution was stirred at −5 °C for 15 min, TLC (SiO_2, CH_2Cl_2/ether (4:1 v/v)) indicated the absence of **44** and the solution was cooled to −78 °C. A 4 M methanol solution of sodium methoxide (2 mL, 8 mmol) was added and the resulting solution was allowed to warm to room temperature. Water was added and the mixture was extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried, and concentrated in vacuo. Purification of the residue by column chromatography (SiO_2, 10 g; eluent, CH_2Cl_2) gave as the major product band 150 mg (50%) of **16a** as a pink oil which crystallized upon standing: mp 80–82 °C, identical by NMR with authentic **16a**.

Method B. A mixture of 0.3 g (1 mmol) of **44** and 0.2 mL of triethylamine in 20 mL of CH_2Cl_2 was refluxed until solution was complete. The solution was cooled to −5 °C and 1.0 mL (1.3 mmol) of a 10% (v/v) CH_2Cl_2 solution of methanesulfonyl chloride was added dropwise. The solution was stirred for 10 min TLC (SiO_2; eluent, CH_2Cl_2/ether (4:1 v/v)) indicated the absence of **44**, and the solution was cooled to −78 °C. By means of a cannula, the solution was added to a solution of 1.5 mL of 40% aqueous NaOH and 2 mL of dioxane in 20 mL of MeOH. The mixture was stirred for 30 min, diluted with water, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried, and concentrated in vacuo. Purification of the residue by column chromatography (SiO_2, 10 g; eluent, CH_2Cl_2) gave 60 mg (21%) of **16a** as a pink oil which crystallized upon standing, mp 80–82 °C. The material was identical in every respect by mp, mmp, and NMR with an authentic sample.

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Registry No. **1a**, 76049-54-2; **1b**, 76049-53-1; **1c**, 76049-52-0; **2a**, 76049-64-4; **2b**, 76049-63-3; **2c**, 76049-61-1; **3a**, 76049-70-2; **3a**·HBr, 101713-47-7; **5a**, 101713-15-9; **5b**, 81078-17-3; **5c**, 81078-16-2; **6a**, 101713-12-6; **6a** (free base), 81078-18-4; **6a**·CH_3SO_3H, 81078-19-5; **6b**, 101713-13-7; **6b** (free base), 89376-31-8; **6b**·CH_3SO_3H, 101713-45-5; **6c**, 101713-14-8; **8a**, 101713-16-0; **8b**, 81078-13-9; **8c**, 81078-12-8; **9a**, 101713-17-1; **9b**, 81078-15-1; **9c**, 81078-14-0; **10a**, 81078-25-3; **10b**, 81078-24-2; **10c**, 81078-23-1; **11a**, 101713-18-2; **11b**, 101713-20-6; **11b**·HCl, 101713-48-8; **12a**, 101713-19-3; **12b**, 101713-21-7; **13a**, 101713-22-8; **13b**, 101713-23-9; **13c**, 81078-28-6; **14a**, 81078-36-6; **14b**, 81078-35-5; **14c**, 81078-32-2; **15a**, 101713-24-0; **15b**, 101713-27-3; **16a**, 81078-37-7; **16b**, 101713-26-2; **16c**, 81078-34-4; **17**, 101713-28-4; **18**, 101713-29-5; **19c**, 81993-61-5; **20c**, 81993-60-4; **21c**, 101713-30-8; **21c** (free base), 101713-49-9; **22c**, 101713-31-9; **23c**, 101713-32-0; **24c**, 101713-33-1; **25a**, 89376-28-3; **25b**, 81993-72-8; **25c**, 81993-71-7; **25c** (dihydropyramidobenzazepine), 101713-46-6; **26b**, 81993-75-1; **27**, 81993-76-2; **28**, 81993-79-5; **29**, 81993-81-9; **30**, 81993-82-0; **30**·HCl, 89376-30-7; **31**, 81993-84-2; **33**, 101713-34-2; **34**, 101713-35-3; **35**, 101713-36-4; **36**, 101713-37-5; **37**, 101713-38-6; **38**, 101713-40-0; **42**, 101713-41-1; **43**, 101713-42-2; **44**, 101713-43-3; **45**, 101713-44-4; acetamidine hydrochloride, 124-42-5; guanidine carbonate, 100224-74-6; 3-(dimethylamino)propylamine, 109-55-7.

Supplementary Material Available: Table III, experimental details of crystals **13a**, **13b**, and **13c**; Table IV, the bond lengths in compounds **13a**, **13b**, and **13c**; Table V, the bond angles in compounds **13a**, **13b**, and **13c**; Tables VI and VII, the final atomic and ansiotropic thermal parameters for **13a**; Tables VIII and IX, the final atomic and anisotropic thermal parameters for **13b**; Table X the final atomic parameters for **13c** (8 pages). Ordering information is given on any current masthead page.

Iminium Ion Mediated Cyclizations of 4-Aryl-1,4-dihydropyridines. Bridging from Nitrogen with Thiophene and an Olefin

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Novel 4-aryl-1,4-dihydropyridines, possessing 2-(3-thienyl)ethyl and 1-buten-4-yl nitrogen substitution, have been prepared by a titanium-promoted Hantzsch-type condensation. Treatment of these dihydropyridines with titanium tetrachloride catalyzes generation of the dihydropyridine/iminium ion. Subsequent trapping of this ion by either the thienyl or the olefinic moiety affords cyclic products derived respectively from elimination or addition pathways available to the intermediate cation. The stereochemistry of these cyclizations is discussed, and the scope of the process is evaluated in light of N-substituted dihydrohydropyridines that do not cyclize.

Several 4-aryl-1,4-dihydropyridines have recently gained clinical importance in the treatment of cardiovascular pathologies, such as angina and hypertension.[1,2] These compounds, which apparently operate by inhibiting the translocation of calcium through the cell membrane, have been termed calcium channel blockers.[3-5]

In addition to the extensive literature describing the chemistry of classical dihydropyridines,[6-11] more recently work has been published which centers on the preparation of novel, conformationally restricted dihydropyridine analogues. In an attempt to relate biological activity to

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