Synthesis of 7-Phenylpyrimido[5,4-*d*][1]benzazepin-2-ones (1)

Wen-Yean Chen and Norman W. Gilman*

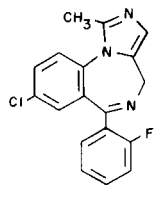
Department of Chemical Research, Hoffmann-La Roche Inc.,
Nutley, New Jersey 07110

Received November 8, 1982

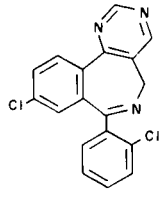
The syntheses of the 7-phenylpyrimido[5,4-*d*][1]benzazepin-2-ones **3, 4,** and **5** are described. The 7-phenyl group was introduced by phenylation of the lactam nitrogen in **10, 13** and **16** respectively. One of these compounds, **5**, showed moderate activity as a CNS agent.

J. Heterocyclic Chem., **20**, 663 (1983).

As part of a medicinal chemistry program designed to develop novel potential central nervous system (CNS) agents, three 7-phenylpyrimido[5,4-*d*][1]benzazepines (compounds **3, 4** and **5**) were synthesized. This novel ring system is a structural variation of annelated 1,4-benzodiazepines such as **1** and of 2-benzazepines such as **2**. Compounds **1** and **2** are currently under clinical investigation as CNS drugs (2,3).

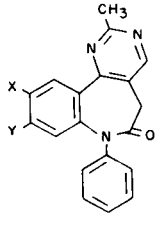


1



2

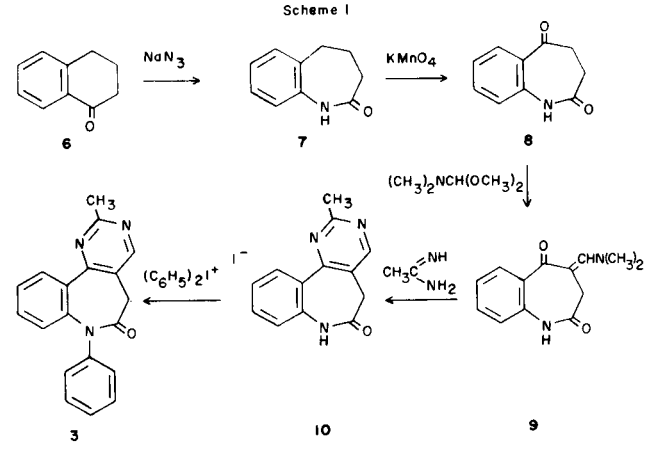
Of the three 7-phenylpyrimido[5,4-*d*][1]benzazepin-2-ones (**3, 4,** and **5**) prepared, compound **5** showed moderate pharmacological activity indicative of a potential CNS anxiolytic agent. All three compounds were prepared from a common starting material, α-tetralone **6**.



3, X = Y = H
4, X = Cl, Y = H
5, X = H, Y = Cl

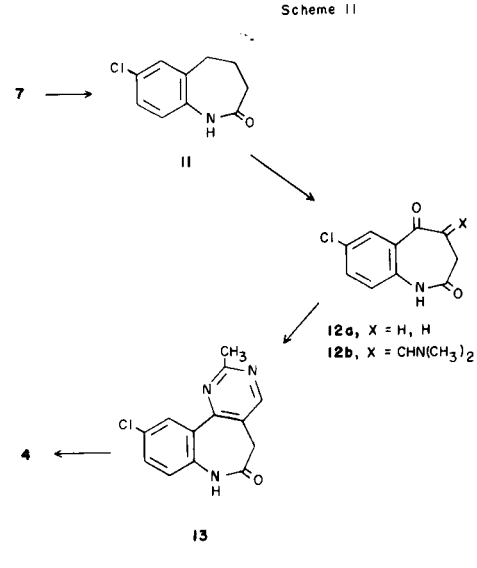
The ring expansion of α-tetralone **6** with sodium azide gave the known (4) lactam **7** (Scheme I) which was oxidized to the ketone **8** with potassium permanganate. Treatment of **8** with dimethylformamide dimethylacetal yielded **9** which was condensed with acetamidine to give the pyrimidine **10**. Phenylation of **10** with diphenyliodonium iodide gave the product **3**.

Scheme I



The preparation of the chloro compound **4** (Scheme II) was accomplished by chlorination of the lactam **7** to give **11**. This chloro-lactam was originally synthesized by Rosowsky (**5**) and co-workers *via* an alternate procedure. The conversion of **11** to **4** was carried out by using the same sequence of reactions as described for the preparation of **3**.

Scheme II

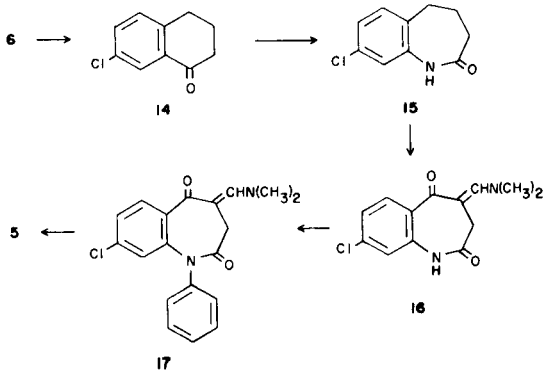


12a, X = H, H
12b, X = CHN(CH$_3$)$_2$

13

Chlorination (6) of α-tetralone afforded the 7-chloro derivative **14** (Scheme III) which was ring expanded (7) and functionalized as before to give **16**. In this instance the phenyl group was introduced before forming the pyrimidine ring since the overall yields were higher by this inversion of the synthetic sequence. Phenylation of **16** gave **17** which when treated with acetamidine gave **5**.

Scheme III



These phenylpyrimido benzazepinones were tested as antagonists (8) of metrazole induced seizures in mice and also as competitive inhibitors of diazepam in the ^{3}H-benzodiazepine receptor binding assay procedure (9). The biological results are shown in the table along with the comparable data for diazepam.

Table

Biolgoical Activity of 1-Benzazepines, **3**, **4** and **5**

Compound	Anti-metrazole ED_{50} mg/kg p.o.	^{3}H-Diazepam Binding IC_{50}, nM
3	>100	780
4	116	>1000
5	9.3	79
Diazepam	1.0	5

EXPERIMENTAL

Melting points were determined on a Reichert hot stage and are uncorrected. Meck silica gel 60, mesh 70-230, was used for all chromatography separations. Either anhydrous sodium sulfate or magnesium sulfate was used for drying of organic solutions. Infrared spectra were determined on a Beckmann IR-9 or a Perkin-Elmer 621 grating spectrometer; mass spectra on a CEC-21-100 instrument; and nuclear magnetic resonance spectra on either a Varian A-60 or HA-100 spectrometer, using tetramethylsilane as a standard.

5,7-Dihydro-2-methyl-7-phenylpyrimido[5,4-*d*][1]benzazepin-6(6*H*)-one (**3**).

To a solution of 2.27 g (10 mmoles) of **10** in 320 ml of dry methanol, heated at 40°, was added 0.567 g (10.5 mmoles) of sodium methoxide. After strirring 20 minutes, 1 g (10 mmoles) of cuprous chloride and 4.08 g (10 mmoles) of diphenyliodonium iodide were added. The mixture was heated under reflux for 3 hours. After cooling, the reaction mixture was concentrated to give an oil which was partitioned between 100 ml of brine and 100 ml of ethyl acetate. The two layers were separated, and the aqueous layer extracted wtih 3 × 50 ml of ethyl acetate. The combined organics were dried and concentrated to give a solid residue which was chromatographed on silica gel (100 g) using methylene chloride-ethyl acetate (2:3) as an eluent. Removal of the solvents gave 2.3 g of crude product which was recrystallized from ethyl acetate and hexane to give 1.6 g (56%) of **3**, mp 172-173°; ms: m/e 301 (M^+); ir (potassium bromide): 1683 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.82 (s, 3H, CH_3), 3.53, 3.72 (AB, J_{gem} = 12.5, 2H, CH_2), 6.90-7.42 (m, 8H, aromatics), 8.03 (m, 1H, aromatic), 8.61 (s, 1H, CH=N).

Anal. Calcd. for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.67; H, 4.85; N, 13.93.

10-Chloro-5,7-dihydro-2-methyl-7-phenylpyrimido[5,4-*d*][1]benzazepin-6(6*H*)-one (**4**).

In 750 ml of dry methanol was suspended 3.4 g (13 mmoles) of **13** and the mixture was heated to 40-50° in an oil bath. Sodium methoxide, 0.74 g (13.6 mmoles) was added. After stirring 20 minutes, 1.3 g (13 mmoles) of cuprous chloride and 5.3 g (13 mmoles) of diphenyliodonium iodide were added. The mixture was heated under reflux for 3 hours, cooled, and filtered. The filtrate was concentrated to remove most of the methanol, and 100 ml of methylene chloride and 50 ml of cold water were added. The two layers were separated and the aqueous layer was extracted with 3 × 10 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated to give 2.5 g of crude **4** which was crystallized from ether and petroleum ether to yield 2.2 g (50%) of **4** as off-white needles, mp 150-152°; ms: m/e 335 (M^+); ir (potassium bromide): 1683 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.82 (s, 3H, CH_3), 3.51, 3.73 (AB, J_{gem} = 12.5, 2H, CH_2), 6.91-7.40 (m, 7H, aromatics), 8.04 (m, 1H, aromatic), 8.63 (s, 1H, CH=N).

Anal. Calcd. for $C_{19}H_{14}ClN_3O$: C, 67.96; H, 4.20; N, 12.51; Cl, 10.56. Found: C, 67.77; H, 4.32; N, 12.28; Cl, 10.31.

9-Chloro-5,7-dihydro-2-methyl-7-phenylpyrimido[5,4-*d*][1]benzazepin-6(6*H*)-one (**5**).

To a mixture of 0.85 g (2.5 mmoles) of **17** in 150 ml of dry methanol was added 0.36 g (3.75 mmoles) of acetamidine hydrochloride. The suspension was stirred at room temperature for 4.5 hours, at which time a clear solution had formed. The reaction mixture was concentrated to remove most of the methanol, and the residue was partitioned between 100 ml of methylene chloride and 50 ml of brine. The two layers were separated and the aqueous layers extracted with 4 × 25 ml of methylene chloride. The combined methylene chloride extracts were dried to give 1.1 g of crude oil which was purified by chromatography on silica gel (100 g). The column was eluted with hexane-ethyl acetate (1:2) to give 0.6 g (71%) of **5**, mp 169-171°. The analytical sample was prepared by recrystallization from ether/petroleum ether to give colorless crystals, mp 169-171°; ms: m/e 335 (M^+); ir (potassium bromide): 1687, 1679 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.81 (s, 3H, CH_3), 3.50, 3.73 (AB, J_{gem} = 12, 1H, CH_2), 6.94-7.46 (m, 7H, aromatics), 8.00 (d, 1H, aromatic), 8.62 (s, 1H, CH=N).

Anal. Calcd. for $C_{19}H_{14}ClN_3O$: C, 67.96; H, 4.20; N, 12.51; Cl, 10.56. Found: C, 67.97; H, 4.31; N, 12.56; Cl, 10.78.

1,3,4,5-Tetrahydro-2*H*-1-benzazepine-2-one (**7**).

Trichloroacetic acid, 150 g (0.92 mole), was melted in a flask on a steam bath and 14.6 g (0.1 mole) of α-tetralone (**6**) and 10 g (0.15 mole) of sodium azide were added. The mixture was occasionally cooled in an ice-water bath and then the mixture was heated on an oil bath at 60-65° for 9 hours with mechanical stirring. The reaction mixture was allowed to stand at room temperature overnight and then 750 ml of cold water was added to the solidified mass. The mixture was stirred for 0.5 hour and filtered. The filter cake was washed with 300 ml of methylene chloride. Water (100 ml) was added, and powdered sodium bicarbonate was added in portions until the aqueous layer became basic. The two layers were separated and the aqueous layer was extracted with 3 × 50 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated to give 9.3 g (57%) of **7**, mp 139-140° (lit mp 139-141°) (4); ir (potassium bromide): 3190 (NH), 1663 cm^{-1} (C=O); nmr (deuterio-

chloroform): δ 2.05-2.48 (m, 4H, CH_2CH_2CO), 2.72-2.82 (m, 2H, $ArCH_2$), 6.90-7.32 (m, 4H, aromatics), 8.20 (bs, 1H, NH).

1,3,4,5-Tetrahydro-2*H*-1-benzazepine-2,5-dione (**8**).

To a solution of 6.44 g (0.04 mole) of **7** in 100 ml of *t*-butyl alcohol were added 300 ml of water, 31.5 g (0.2 mole) of potassium permanganate and 51 g (0.2 mole) of magnesium nitrate hexahydrate. The mixture was stirred at room temperature in a water bath for 20 hours. The reaction mixture was cooled, 200 ml of 3*N* hydrochloric acid was added, followed by adding sodium bisulfite in portions until the mixture became a clear yellow solution. The solution was extracted with 3 × 100 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated to give 3.1 g (44%) of crude solid which was recrystallized from ethyl acetate and hexane to give 1.84 g (26%) of **8**, mp 183-185°. The analytical sample was prepared by recrystallization from the same solvents and obtained as colorless needles, mp 185-186°; ms: m/e 175 (M^+); ir (potassium bromide): 3325, 3225 (NH), 1682 (C=O), 1668 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.79-2.97 (m, 4H, CH_2CH_2), 7.04-7.28 (m, 2H, aromatics), 7.38-7.60 (m, 1H, aromatic), 7.88-8.02 (m, 1H, aromatic), 9.73 (bs, 1H, NH).

Anal. Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.54; H, 5.14; N, 7.92.

4-[(Dimethylamino)methylidene]-1,3,4,5-tetrahydro-2*H*-1-benzazepine-2,5-dione (**9**).

A mixture of 1.4 g (8.0 mmoles) of **8** and 30 ml of *N,N*-dimethylformamide dimethylacetal was heated in an oil bath at 115-120° for 1 hour. After cooling, ether was added and the precipitated product was collected by filtration. The yield was 1.6 g (87%), mp 218-220°; ms: m/e 230 (M^+); ir (potassium bromide): 3190 (NH), 1670 (C=O), 1648 cm^{-1} (C=O); nmr (DMSO-d_6): δ 3.25 (s, 8H, $(CH_3)_2$, CH_2), 6.94-7.68 (m, 5H, aromatics, C=CH), 9.85 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.62; H, 6.02; N, 12.38.

2-Methyl-5,7-dihydropyrimido[5,4-*d*][1]-benzazepin-6(6*H*)-one (**10**).

To a mixture of 5.4 g (23.4 mmoles) of **9** and 3.3 g (35 mmoles) of acetamidine hydrochloride in 200 ml of dry methanol was added 3.8 g (70 mmoles) of sodium methoxide. After stirring 2.5 hours at room temperature, 100 ml of cold water was added. The mixture was extracted with 3 × 100 ml of methylene chloride, and the combined methylene chloride solutions were dried and concentrated to give **10** which was recrystallized from ethyl acetate and hexane to give 4.4 g (83%) of **10** as colorless needles, mp 257-258°; ms: m/e 225 (M^+); ir (potassium bromide): 3200 (NH), 1689 cm^{-1} (C=O); nmr (DMSO-d_6): δ 2.69 (s, 3H, CH_3), 3.43 (s, 2H, CH_2), 7.16-7.62 (m, 3H, aromatics), 8.04-8.12 (m, 1H, aromatic), 8.65 (s, 1H, CH=N).

Anal. Calcd. for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.65. Found: C, 69.00; H, 4.67; N, 19.01.

7-Chloro-1,3,4,5-tetrahydro-2*H*-1-benzazepine-2-one (**11**).

To a solution of 7.5 g (46.5 mmoles) of **7** in 23 ml of glacial acetic acid was added dropwise a solution of 3.6 g (51 mmoles) of chlorine gas in 30 ml of glacial acetic acid. The reaction was cooled in a cold water bath with stirring during the addition. After 30 minutes, a white precipitate formed. The mixture was stirred another 2.5 hours and quickly filtered. The precipitate was dissolved in 200 ml of methylene chloride, 100 ml of water was added and then sodium bicarbonate powder was added with stirring until all the residual acetic acid was neutralized. The two layers were separated and the aqueous layer extracted with 3 × 50 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated. The solid residue was crystallized from ethyl acetate and hexane to give 5.1 g (56%) of **11** as colorless needles, mp 164-166°; ms: m/e 195 (M^+); ir (potassium bromide): 3175 (NH), 1684 cm^{-1} (C=O); nmr (DMSO-d_6): δ 1.98-2.24 (m, 4H, CH_2CH_2), 2.65 (m, 2H, CH_2), 6.88-7.35 (m, 3H, aromatics), 9.48 (bs, 1H, NH).

Anal. Calcd. for $C_{10}H_{10}ClNO$: C, 61.39; H, 5.15; N, 7.16; Cl, 18.12. Found: C, 61.34; H, 5.13; N, 7.22; Cl, 18.10.

7-Chloro-1,3,4,5-tetrahydro-2*H*-1-benzazepine-2,5-dione (**12a**).

The 7-chlorolactam **11** (5.5 g, 27 mmoles) was dissolved in 150 ml of *t*-butanol and then 300 ml of water, 21.3 g (135 mmoles) of potassium permanganate and 34.6 g (135 mmoles) of magnesium nitrate hexahydrate were added. The mixture was stirred at room temperature in a water bath for 20 hours. The reaction mixture was cooled, 200 ml of 3*N* hydrochloric acid was added followed by adding sodium bisulfite until the pink color of the solution changed to yellow. The solution was extracted with 3 × 100 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated to give 2.5 g (47%) of crude solid which was crystallized from ethyl acetate and hexane to give 1.6 g (28.5%) of **12a**, as colorless needles, mp 201-206°. The analytical sample was prepared by recrystallization from the same solvents, mp 215-216°; ms: m/e 209 (M^+); ir (potassium bromide): δ 3220 (NH), 1670 cm^{-1} (C=O); nmr (DMSO-d_6): δ 2.58-3.00 (m, 4H, CH_2CH_2), 7.10-7.76 (m, 3H, aromatics).

Anal. Calcd. for $C_{10}H_8ClNO_2$: C, 57.30; H, 3.85; N, 6.68; Cl, 16.91. Found: C, 57.30; H, 3.97; N, 6.78; Cl, 17.10.

7-Chloro-4-[(dimethylamino)methylidene]-3,4-dihydro-1*H*-1-benzazepin-2,5-dione (**12b**).

A mixture of 3.0 g (14.3 mmoles) of **12a** and 50 ml of *N,N*-dimethylformamide dimethylacetal was heated at 115-120° on an oil bath. After 1 hour the reaction mixture was cooled and filtered. The collected solid was washed with ether to give 1.7 g (45%) of **12b**, mp 225-230°. The analytical sample was obtained as a yellow solid by recrystallization from ethyl acetate, mp 232-234°; ms: m/e 264 (M^+); ir (potassium bromide): 3195 (NH), 1678 (C=O), 1638 cm^{-1} (C=O); nmr (DMSO-d_6): δ 3.21 (s, 6H, $(CH_3)_2$), 3.26 (s, 2H, CH_2), 7.02-7.62 (m, 4H, aromatics, C=CH), 9.97 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58. Found: C, 59.27; H, 5.03; N, 10.61.

10-Chloro-2-methyl-5,7-dihydropyrimido[5,4-*d*][1]benzazepin-6(6*H*)-one (**13**).

To a mixture of 3.8 g (14.4 mmoles) of **12b** and 2.05 g (21.6 mmoles) of acetamidine hydrochloride in 100 ml of dry methanol was added 2.35 g (43.2 mmoles) of sodium methoxide. After stirring 2.5 hours at room temperature, 100 ml of water was added and the mixture extracted with 3 × 100 ml of methylene chloride. The combined methylene chloride solutions were dried and concentrated to give **13** which was recrystallized from ethyl acetate and hexane to give 3.4 g (90%). The analytical sample was obtained as a colorless powder from the same solvents, mp 293-295°; ms: m/e 259 (M^+); ir (potassium bromide): 3190 (NH), 1682 cm^{-1} (C=O); nmr (DMSO-d_6): δ 2.67 (s, 3H, CH_3), 3.47 (s, 2H, CH_2), 7.24-7.97 (m, 3H, aromatics), 8.72 (s, 1H, CH=N), 10.41 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{10}ClN_3O$: C, 60.13; H, 3.88; N, 16.18; Cl, 13.65. Found: C, 60.18; H, 3.82; N, 16.02; Cl, 13.40.

7-Chloro-α-tetralone (**14**).

A suspension of 23.7 g (76 mmoles) of silver sulfate in 150 ml of concentrated sulfuric acid and 24 ml of water was mechanically stirred for 0.5 hour and then 22.2 g (152 mmoles) of α-tetralone was added. A cold solution of 11.3 g (160 mmoles) of chlorine in 200 ml of carbon tetrachloride was then added dropwise. The temperature was kept below 20° during the addition. After the addition (*ca.* 1 hour), the mixture was stirred for another 2 hours. The reaction mixture was poured into 500 g of ice and then filtered to remove silver chloride. The filtrate layers were separated, and the aqueous layer was extracted with 3 × 100 ml of methylene chloride. The combined organic solutions were washed with a saturated solution of sodium bicarbonate, dried and concentrated. The residue was chromatographed on 1 kg of silica gel using hexane-ethyl acetate (9:1) as the eluent. Evaporation of the solvents gave 10 g (55%) of **14**, mp 92-94° (lit (6) mp 98-98.5°); nmr (deuteriochloroform): δ 2.11 (q, 2H, CH_2), 2.63 (t, 2H, CH_2), 2.92 (t, 2H, CH_2), 7.10-7.52 (m, 2H, aromatics), 7.97 (d, 1H, aromatic).

8-Chloro-1,3,4,5-tetrahydro-2*H*-benzazepine-2-one (**15**).

To 180 g (1.1 moles) of trichloroacetic acid heated in a flask on a steam bath was added 16 g (0.088 mole) of 7-chloro-α-tetralone (**14**) and 9.65 g (0.148 mole) of sodium azide. The mixture was occasionally cooled in an ice-water bath and then heated in an oil bath at 60-65° for 6 hours with mechanical stirring. The reaction mixture was allowed to stand at room temperature overnight and then 1.5 ℓ of water was added to the solidified mass. The white turbid mixture was extracted with 3 × 300 ml of methylene chloride. To the combined methylene chloride solution was added 300 ml of water and then sodium bicarbonate in portions until the aqueous layer turned basic. The two layers were separated and the aqueous layer extracted with 3 × 100 ml of methylene chloride. The combined methylene chloride extracts were dried and concentrated to give a crude oil which was crystallized from ethyl acetate to give 2.2 g of **15**, mp 135-139°. The mother liquor was concentrated and the residue chromatographed on silica gel (600 g) using hexane-ethyl acetate (1:1) as an eluent, to give 7.4 g of **15**, mp 140-142° (lit (10) mp 157-158°). The total yield was 9.6 g (55%); nmr (deuteriochloroform): δ 2.30 (m, 4H, CH_2CH_2), 2.86 (t, 2H, CH_2), 7.01-7.24 (m, 3H, aromatics), 8.43 (bs, 1H, NH).

8-Chloro-4-[(dimethylamino)methylidene]-3,4-dihydro-1*H*-1-benzazepine-2,5-dione (**16**).

To a solution of 9.6 g (49 mmoles) of **15** in 250 ml of *t*-butyl alcohol was added 500 ml of water, 38.7 g (245 mmoles) of potassium permanganate and 63 g (245 mmoles) of magnesium nitrate hexahydrate. The mixture was stirred at room temperature for 20 hours, cooled, and 250 ml of 3*N* hydrochloric acid was added, followed by sodium bisulfite until the pink color of the solution changed to yellow. The solution was extracted with 3 × 200 ml of methylene chloride. The combined methylene chloride extracts were dried and concentrated to give 2.73 g (27%) of 8-chloro-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2,5-dione, mp 206-209°, which was used without further purification.

A mixture of 2.1 g (10 mmoles) of the above dione and 25 ml of *N,N*-dimethylformamide dimethylacetal was heated at 115-120° in an oil bath for 1 hour. The reaction mixture was cooled and filtered. The solid was washed with ether to give 0.4 g (15%) of **16**. The analytical sample was obtained as a beige solid by trituration with ether, the mp 288-290°; ms: m/e 264 (M^+); ir (potassium bromide): 1680 (C=O), 1650 cm^{-1} (C=O); nmr (DMSO-d): δ 3.23 (s, 8H, $N(CH_3)_2$ and CH_2), 7.07-7.69 (m, 4H, aromatics and =CH), 9.98 (bs, 1H, NH).

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58; Cl, 13.39. Found: C, 59.12; H, 5.12; N, 10.15; Cl, 13.09.

8-Chloro-1-phenyl-4-[(dimethylamino)methylidene]-3,4-dihydro-1*H*-1-benzazepine-2,5-dione (**17**).

A suspension of 2.0 g (7.6 mmoles) of **16** in 750 ml of dry methanol was heated at 50-60° in an oil bath for 0.5 hour and then cooled to 40°. After adding 0.47 g (8.7 mmoles) of sodium methoxide, the mixture was heated to 50-60° for 0.5 hour and then cooled to 40°. After adding 0.76 g (7.6 mmoles) of cuprous chloride and 3.26 g (8 mmoles) of diphenyliodonium iodide, the mixture was heated under reflux for 3 hours and then cooled and filtered. The filtrate was concentrated and the residue was chromatographed on silica gel (100 g) and eluted with ethyl acetate to give 0.75 g (29%) of **17**, mp 242-243°. The analytical sample was obtained as pale yellow plates by recrystallization from ethyl acetate, mp 242-243°; ms: m/e 340 (M^+); ir (potassium bromide): 1677 (C=O); 1642 cm^{-1} (C=O); nmr (DMSO-d_6): δ 3.25 (s, 6H, $N(CH_3)_2$), 3.20, 3.72 (AB, J_{gem} = 14 Hz, 2H, CH_2), 6.69-7.71 (m, 8H, aromatics and =CH).

Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 5.03; N, 8.22; Cl, 10.40. Found: C, 66.69; H, 5.31; N, 7.97; Cl, 10.16.

Acknowledgement.

The authors are grateful to the following members of our Department of Physical Chemistry under Dr. R. P. W. Scott: Mr. S. Traiman (ir spectra), Dr. T. Williams (nmr spectra), Dr. W. Benz (mass spectra) and Dr. F. Scheidl (microanalytical data).

REFERENCES AND NOTES

(1) Dedicated to the memory of Dr. Willy Leimgruber, deceased July 8, 1981.

(2) For the synthesis of **1**, see: A. Walser, L. E. Benjamin, Sr., T. Flynn, C. Mason, R. Schwartz and R. Ian Fryer, *J. Org. Chem.*, **43**, 936 (1978).

(3) For the chemistry of 2-benzazepines relating to compound **2** see: E. J. Trybulski, L. E. Benjamin, Sr., J. Early, R. I. Fryer, N. Gilman, E. Reeder, A. Walser, W. Dairman, A. Davidson, W. Horst, R. O'Brien, J. Sepinwall; submitted to *J. Med. Chem.*,

(4) Prepared by the method of P. A. S. Smith, *J. Am. Chem. Soc.*, **70**, 320 (1948).

(5) A. Rosowsky, M. Chaykowsky, S. A. Yeager, R. A. St. Amand, M. Lin and E. J. Modest, *J. Heterocyclic Chem.*, **8**, 809 (1971).

(6) The method of J. H. Gorvin, *Chem. Ind. (London)*, 910 (1951) was used for the chlorination. 7-Chloro-1-tetralone has been prepared by the other methods, see: *Chem. Abstr.*, **72**, 66702y (1970).

(7) The chloro-lactam **15** has been prepared by alternate methods: O. Aki and Y. Nakagawa, *Chem. Pharm. Bull.*, **20**, 1325 (1972).

(8) The authors thank Dr. W. Dairman and his staff of our Toxicology Department for the determination of the metrazole data.

(9) The binding assays were determined by Drs. W. D. Horst, R. A. O'Brien and their co-workers in our Pharmacology II Department.

(10) M. Tomita, S. Minami and S. Uyeo, *J. Chem. Soc. (C)*, 183 (1969).