Synthesis of 1,4-Dihydro-4-methyl-1-phenyl-5*H*-1,3,4-benzotriazepin-5-ones

Norton P. Peet and Shyam Sunder*

Pharmaceutical Research and Development - Medicinal Chemistry, Building 438,
The Dow Chemical Company, Midland, Michigan 48640

Received June 2, 1976

The synthesis of 1,4-dihydro-4-methyl-1-phenyl-5*H*-1,3,4-benzotriazepin-5-one (**4a**) and its 8-chloro analog (**4b**) is described. Attempted synthesis of the 2-methyl analog of **4a** from 2-(phenylamino)benzoic acid 1-methylhydrazide (**10**) and triethyl orthoacetate led only to the Schiff base intermediate, 2-(phenylamino)benzoic acid 2-(1-ethoxyethylidene)-1-methylhydrazide (**11**). Cyclization of **11** was attempted unsuccessfully with a variety of reagents. The interesting reaction products from the treatment of **11** with trifluoroacetic acid are described.

J. Heterocyclic Chem., 13, 967 (1976).

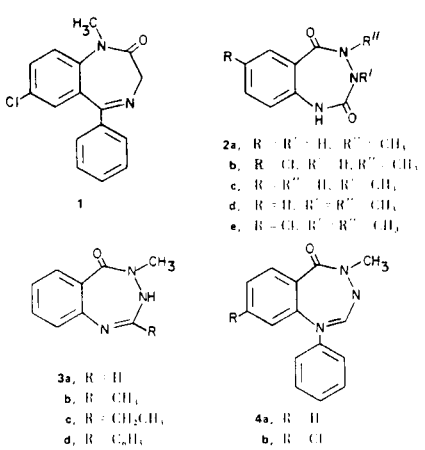
The 1,4-benzodiazepines are an important class of compounds, several of which are currently being used as psychotherapeutic agents (1). One representative of this class which has enjoyed widespread clinical use and has encouraged a great deal of synthetic effort is 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (**1**) or diazepam (generic name).

The considerable interest in 1,4-benzodiazepines as medicinal agents has also generated synthetic interest in benzotriazepine systems. We have recently developed new routes to 3,4-dihydro-1*H*-1,3,4-benzotriazepine-2,5-diones and have reported compounds **2a-e** (2). Our continuing efforts in this area led us to prepare 3,4-dihydro-5*H*-1,3,4-benzotriazepin-5-ones **3a-d**, one (**3d**) of which contains a 2-phenyl substituent (3). From a biological standpoint we felt that a 1-phenyl substituent on the benzotriazepine nucleus would be most desirable, since the pharmacologically active 1,4-benzodiazepines have phenyl or substituted-phenyl substituents at the 5-position. Therefore, we set out to prepare benzotriazepinones **4a** and **b** (Scheme I). This report describes the syntheses of **4a** and **b** and related chemistry.

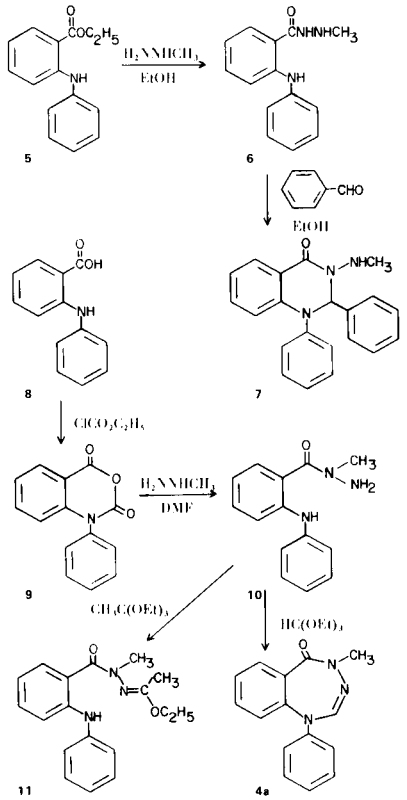
The intermediate which we envisioned for the preparation of benzotriazepinone **4a** was hydrazide **10**. Thus, *N*-phenylisatoic anhydride (**9**) was prepared from *N*-phenylanthranilic acid (**8**) and ethyl chloroformate as described (4). Treatment of **9** with methylhydrazine afforded hydrazide **10**. That hydrazide **10** could not be produced from an acylating agent less reactive than anhydride **9** was demonstrated by treating ethyl *N*-phenylanthranilate (**5**) with methylhydrazine in ethanol. The reaction was sluggish, requiring two weeks for completion, and yielded 2-(phenylamino)benzoic acid 2-methylhydrazide (**6**). It has been shown that methylhydrazine reacts with acetic anhydride to yield predominantly 1-acetyl-1-methylhydrazine, and with ethyl acetate to yield predominantly 1-acetyl-2-methylhydrazine (5). Derivatization of **6** with benzaldehyde yielded dihydroquinazolinone **7**.

Cyclization of hydrazide **10** with triethyl orthoformate proceeded smoothly to give 1,4-dihydro-4-methyl-1-phenyl-5*H*-1,3,4-benzotriazepin-5-one (**4a**), which was a bright yellow crystalline material. Attempted cyclization with triethyl orthoacetate, however, yielded 2-(phenylamino)-benzoic acid 2-(1-ethoxyethylidene)-1-methylhydrazide

Scheme I



Scheme II



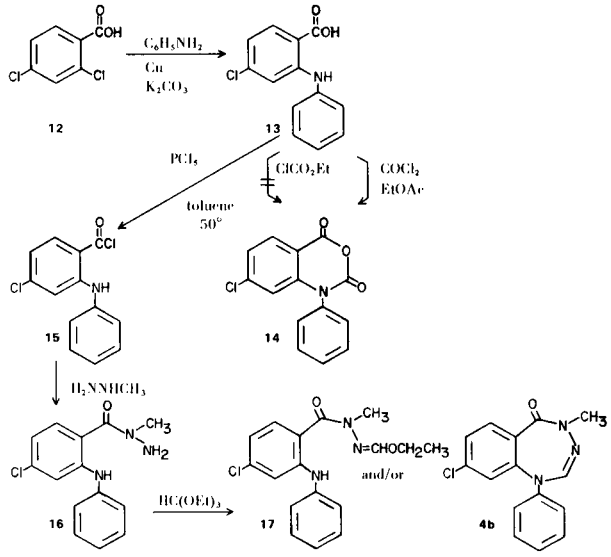
(**11**) rather than the 2-methyl analog of **4a**. See Scheme II.

In order to prepare the 4-chloro analog of **4a** (**4b**), we attempted the preparation of the unreported 4-chloro-*N*-phenylisatoic anhydride (**14**) using the same procedure we had employed for the preparation of **9**. 4-Chloro-*N*-phenylanthranilic acid (**13**), which was prepared from 2,4-dichlorobenzoic acid (**12**) and aniline in the presence of potassium carbonate and copper powder(6), was unchanged after heating at reflux in excess ethyl chloroformate for 18 hours. Treatment of **13** with one equivalent of ethyl chloroformate in pyridine at reflux for 18 hours led only to recovered **13** and a mixture of other products which did not appear to contain **14**. These results exemplify the deactivating effect of the 4-chloro group on the diphenylamino nitrogen atom of **13**.

To circumvent the need for **14**, we prepared 4-chloro-2-(phenylamino)benzoyl chloride (**15**) by treating **13** with phosphorus pentachloride in toluene (7). It was necessary to carefully monitor the temperature of this reaction, since 2-(phenylamino)benzoyl chlorides thermally decompose to acridones (8). Treatment of **15** with methylhydrazine yielded 4-chloro-2-(phenylamino)benzoic acid 1-methylhydrazide (**16**). It was only at this point when we discovered that **14** could be prepared by treating **13** with excess phosgene in ethyl acetate for several days at room temperature. See Scheme III.

Cyclization of hydrazide **16** to **4b** was a sluggish reaction, which proceeded through the intermediate Schiff base **17**. The reaction of **16** with triethyl orthoformate was monitored by tlc: short reaction times yielded pre-

Scheme III



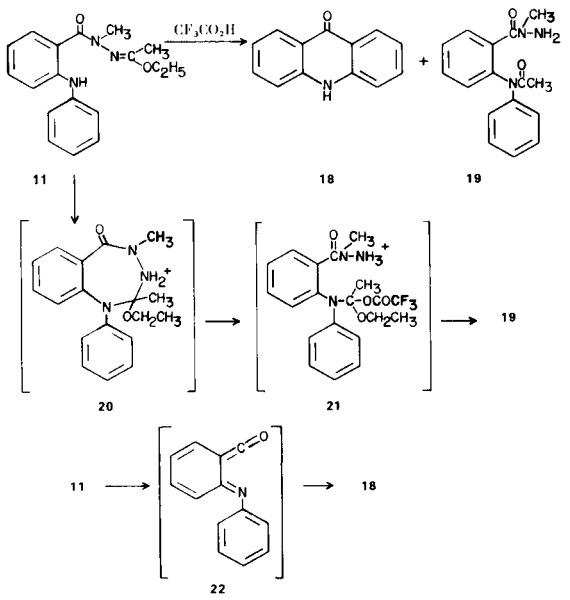
dominantly **17** while long reaction times yielded predominantly **4b**. When a sample of pure **4b** was treated with triethyl orthoformate and ethanol at reflux for 48 hours, the formation of **17** was not observed, which ruled out the possibility that an equilibrium between **17** and **4b** was being established. Thus, the cyclization of **17** to **4b** was a slow reaction, and the deactivating effect of the 4-chloro group on the diphenylamino nitrogen atom of **17** was again significant.

As mentioned earlier, treatment of hydrazide **10** with triethyl orthoacetate led only to Schiff base **11**. Several reagents and reaction conditions were employed in an attempt to cyclize hydrazide **11** to the 2-methyl analog of **4a**. Heating **11** (m.p. 82-83°) neat at 160° (1 hour) or in decalin at reflux (2 hours) led only to the isolation of a different crystalline form of **11** (m.p. 91-92°). Heating **11** in Dowtherm A at 245° (2 hours) led to an intractable mixture of products, as did the treatment of **11** with boron trifluoride etherate. Treatment of **11** with potassium *t*-butoxide in *t*-butanol at reflux (15 hours) yielded only unchanged **11**.

Scheme IV shows the two products that were isolated after a solution of **11** in trifluoroacetic acid was heated at reflux (15 hours). The structure of **18**, 9(10*H*)acridone (9), was indicated on the basis of spectral data, combustion analysis, and by comparison with an authentic sample. 9(10*H*)Acridone (**18**) could arise from intermediate **22**, which, in turn, could be produced from **11** by a protona-

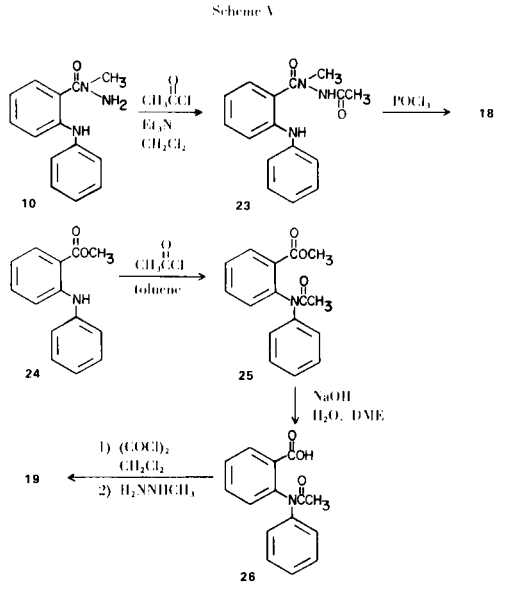
tion-elimination sequence. 2-(Acetylphenylamino)benzoic acid 1-methylhydrazide (**19**) could arise from **11** *via* intermediate **20**, which, instead of undergoing elimination of ethanol to yield the (protonated) 2-methyl analog of **4a**, cleaves to intermediate **21**, which yields **19** upon hydrolysis.

Scheme IV



The identity of compound **19** was indicated by its dissimilarity to 2-(phenylamino)benzoic acid 1-methyl-2-acetylhydrazide (**23**), and by its alternate preparation (Scheme V). Thus, acetylation of **10** with acetyl chloride yielded hydrazide **23**, which was distinctly different from **19**. (Subsequent treatment of **23** with phosphorus oxychloride yielded **18**.) An alternate synthesis of **19** was initiated from methyl *N*-phenylanthranilate (**24**), which was converted to methyl 2-(acetylphenylamino)benzoate (**25**) with acetyl chloride in toluene. Hydrolysis of **25** with aqueous base produced 2-(acetylphenylamino)benzoic acid (**26**). Brief treatment of **26** with an equivalent of oxalyl chloride followed by quenching with methylhydrazine yielded a mixture of products from which **19** was isolated by thick layer chromatography.

Scheme V



We conclude that we were unable to prepare the 4-methyl analog of **4a** from Schiff base **11** for steric reasons. It is interesting to note that in the conversion of **11** to **19**, a triazepinone intermediate (**20**) which must be produced does not lead to the desired cyclized product. Perhaps intermediate **20**, and the protonated 2-methyl analog of **4a** with which it may be in equilibrium, are high-energy intermediates which are unstable with respect to acyclic intermediate **21** due to steric interactions.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded with a Perkin-Elmer Model 727 Spectrophotometer, nmr spectra with Varian T-60 and Perkin-Elmer R32 (90 MHz) spectrometers, and mass spectra with a Hitachi RMU-6D mass spectrometer (70 eV). Combustion analyses for C, H, and N were performed by Dow Analytical Laboratories.

Materials.

Ethyl *N*-phenylanthranilate (**5**), b.p. 162° (2.5 mm) [lit. (10) b.p. 184-187° (6.0 mm)] and methyl *N*-phenylanthranilate (**23**), b.p. 140° (0.10 mm), m.p. 53-56° [lit. (11a) m.p. 57-58°; lit. (11b) m.p. 58-59°] were prepared from **8** using standard esterification procedures. *N*-Phenylisatoic anhydride (**9**), m.p. 174-175° [lit. (4) m.p. 177-179°] was prepared from **8** and ethyl chloroformate as described by Santilli (4). 4-Chloro-*N*-phenylanthranilic acid (**13**), m.p. 190-194° [lit. (6a) m.p. 198-200°; lit. (6b) m.p. 201°] was prepared from **12** using the method of Cherntsov (6b). 4-Chloro-2-(phenylamino)benzoyl chloride (**15**), m.p. 102-103° [lit. (7) m.p. 102-103°] was prepared from **13** using the procedure described by Grigorovskii (7).

2-(Phenylamino)benzoic Acid 2-Methylhydrazide (**6**).

A 48.2-g. (0.200 mole) quantity of **5** and 23.0 g. (0.500 mole) of methylhydrazine (Aldrich) in 200 ml. of ethanol were heated at reflux for 14 days, at which time tlc indicated the absence of **5**. The reaction solution was evaporated to dryness. The resulting oil was redissolved in methylene chloride and evaporated to dryness; this process was twice repeated. The resulting thick oil was triturated with ether to produce a white solid, which was collected and air-dried to afford 30.1 g. (62%) of **6**; m.p. 104-105°; ir (Nujol): 3280 (broad, NH), 1640 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 9.15 (broad s, 1H, NH), 8.27 (broad s, 1H, NH), 7.50-6.53 (m, 9H, aromatic), 4.60 (broad s, 1H, NH), 2.70 (s, 3, CH_3).

Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.42. Found: C, 69.96; H, 6.33; N, 17.34.

1,2-Dihydro-3-(methylamino)-1,2-diphenyl-4(3*H*)quinazolinone (**7**).

A solution of a 6.03-g. (25.0 mmoles) quantity of **6** and 2.65 g.

(25.0 mmoles) of benzaldehyde in 25 ml. of ethanol were heated at reflux for 48 hours. The solution was concentrated to a thick oil, which crystallized upon standing for several days. The crystals were slurried with ether-hexane, collected, and recrystallized from ether-hexane to afford 2.70 g. (33%) of **7**, m.p. 94-95°; ir (Nujol): 3270 (NH), 1640 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 8.13-7.95 (m, 1H, H *ortho* to C=O), 7.60-6.87 (m, 13H, remaining aromatic), 6.18 (s, 1H, methine), 5.20 (broad s, 1H, NH, deuterium oxide exchangeable), 2.60 (s, 3H, CH_3); mass spectrum: (70 eV) m/e 329 (molecular ion).

Anal. Calcd. for $C_{21}H_{19}N_3O$: C, 76.57; H, 5.81; N, 12.76. Found: C, 76.24; H, 5.74; N, 12.57.

2-(Phenylamino)benzoic Acid 1-Methylhydrazide (**10**).

A 68.7-g. (0.287 mole) quantity of *N*-phenylisatoic anhydride (Aldrich) in 100 ml. of dry dimethylformamide was placed in an oilbath which was maintained at 50-55°. A solution of 13.8 g. (0.300 mole) of methylhydrazine in 50 ml. of dimethylformamide was added dropwise over a 20-minute period. After the cessation of gas evolution, the reaction solution was stirred at 50-55° for 1 hour and then concentrated to a thick oil. Seed crystals were obtained by evacuating a portion of the oil to 0.5 mm at 70°. The remainder of the oil was seeded and triturated with ether to produce a white solid which was collected and air-dried to afford 44.0 g. (63%) of **10**, m.p. 106-107° [m.p. 106-107° (ethanol)]; ir (Nujol): 3250 and 3170 (NH and NH_2), 1635 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 7.50-6.77 (m, 10H, aromatic and NH), 4.54 (broad s, 2, NH_2), 3.23 (s, 3, CH_3).

Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.42. Found: C, 69.90; H, 6.31; N, 17.26.

1,4-Dihydro-4-methyl-1-phenyl-5*H*-1,3,4-benzotriazepin-5-one (**4a**).

A 5.00-g. (20.7 mmoles) quantity of **10** and 7 ml. of triethyl orthoformate (Aldrich) were heated at reflux for 3.5 hours. Tlc indicated the absence of **10** and a single product. The reaction solution was concentrated to a thick oil which solidified upon trituration with ether. The solid was collected to yield 2.62 g. (50%) of **4a**; m.p. 108-109° (ethanol; pale green prisms): ir (Nujol): 1660 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 8.06-7.83 (m, 1H, H *ortho* to C=O), 7.53-7.02 (m, 8H, aromatic and methine), 6.60-6.38 (m, 1H, H *ortho* to N), 3.45 (s, 3H, CH_3).

Anal. Calcd. for $C_{15}H_{13}N_3O$: C, 71.69; H, 5.21; N, 16.72. Found: C, 71.80; H, 5.23; N, 16.79.

2-(Phenylamino)benzoic Acid 2-(1-Ethoxyethylidene)-1-methylhydrazide (**11**).

A 10.0-g. (41.0 mmoles) quantity of **10** and 10 ml. of triethyl orthoacetate (Aldrich) were heated at reflux for 72 hours. The reaction solution was cooled and the resulting white, crystalline solid was collected, washed with ether and air-dried to yield 11.2 g. (88%) of **11**, m.p. 89-90° [m.p. 91-92° (ethanol)]; ir (Nujol): 3350 (NH), 1610 (C=O) cm^{-1}; nmr: δ 7.57-6.57 (m, 10H, aromatic and NH), 4.15 (q, J = 7 Hz, 2H, CH_2), 3.23 (s, 3, NCH_3), 1.82 (s, 3H, CCH_3), 1.23 (t, J = 7 Hz, 3H, CH_2CH_3).

Anal. Calcd. for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.50. Found: C, 69.64; H, 6.90; N, 13.25.

7-Chloro-1-phenyl-2*H*-3,1-benzoxazine-2,4(1*H*)dione (**14**).

To a solution of 2.48 g. (10.0 mmoles) of **13** in 50 ml. of ethyl acetate was added 20 ml. of phosgene. After 6 days, an ir of a concentrated aliquot indicated the absence of **14**. The solution was concentrated to yield 2.74 g. (quantitative yield) of **14**, m.p. 209-210° (ethanol; gray needles); ir: 1780 and 1730 (C=O) cm^{-1}; nmr (DMSO-d_6): δ 8.10 (d of d, J = 7 Hz and 2 Hz, 1H, H *ortho* to C=O), 7.91-7.28 (m, 6H, aromatic), 6.47-6.30 (d, J = 2 Hz, 1H, H *meta* to C=O, *ortho* to N).

Anal. Calcd. for $C_{14}H_8ClNO_3$: C, 61.44; H, 2.95; N, 5.12. Found: C, 61.40; H, 3.16; N, 5.17.

4-Chloro-2-(phenylamino)benzoic Acid 1-Methylhydrazide (**16**).

To a solution of 12.6 g. (47.3 mmoles) of **15** in 100 ml. of methylene chloride was added, dropwise over a period of 15 minutes, 10 ml. of methylhydrazine in 50 ml. of methylene chloride. The addition was exothermic. After 45 minutes, the solution was washed with water, dried (sodium sulfate) and concentrated to yield 13.0 g. (quantitative yield) of **16**, m.p. 130-132° (ethanol); ir (Nujol): 3230 and 3160 (NH and NH_2), 1640 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 7.42 (broad s, 1H, NH, deuterium oxide exchangeable), 7.39-6.94 (m, 7H, aromatic), 6.74 (d of d, J = 8 Hz and 2 Hz), 4.40 (broad s, 2H, NH_2, deuterium oxide exchangeable), 3.21 (s, 3H, CH_3).

Anal. Calcd. for $C_{14}H_{14}ClN_3O$: C, 60.98; H, 5.12; N, 15.23. Found: C, 60.74; H, 5.17; N, 15.06.

4-Chloro-2-(phenylamino)benzoic Acid 2-(1-Ethoxymethylidene)-1-methylhydrazide (**17**).

A 3.00-g. (10.8 mmoles) quantity of **16** and 20 ml. of triethyl orthoformate were heated at reflux for 90 minutes. Tlc indicated the absence of **16** and one major product. The solution was concentrated and the viscous oil was triturated with ether to produce a white solid which was collected, washed with ether and air-dried to afford 2.40 g. (67%) of **17**, m.p. 110-112° [m.p. 111.5-112.5° (ethanol)]; ir (Nujol): 3300 (NH), 1620 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 7.57 (s, 2H, NH and methine, reduces to 1H sharper s with deuterium oxide), 7.37-6.83 (m, 7H, aromatic), 6.64 (d of d, J = 8 Hz and 2 Hz, H *meta* to C=O and *ortho* to N), 3.93 (q, J = 7 Hz, 2H, CH_2), 3.33 (s, 3H, NCH_3), 1.23 (t, J = 7 Hz, 3H, CH_2CH_3).

Anal. Calcd. for $C_{17}H_{18}ClN_3O_2$: C, 61.53; H, 5.46; N, 12.66. Found: C, 61.80; H, 5.47; N, 12.65.

8-Chloro-1,4-dihydro-4-methyl-1-phenyl-5*H*-1,3,4-benzotriazepine-5-one (**4b**).

A 5.00-g. (18.1 mmoles) quantity of **16** and 25 ml. of triethyl orthoformate were heated at reflux for 4 days. Tlc indicated the absence of **16**, a small spot corresponding to **17**, and one major product. The yellow solution was concentrated and the resulting yellow solid was recrystallized from ethanol to yield 3.10 g. (60%) of **4b**, m.p. 160-161° (bright yellow needles); ir (Nujol): 1650 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 7.90 (d, J = 8 Hz, 1H, H *ortho* to C=O), 7.70-6.90 (m, 7H, aromatic and methine), 6.40 (d, J = 2 Hz, 1H, H *meta* to C=O and *ortho* to N), 3.44 (s, 3H, CH_3); mass spectrum: (70 eV) m/e 285 (molecular ion).

Anal. Calcd. for $C_{15}H_{12}ClN_3O$: C, 63.50; H, 4.23; N, 14.70. Found: C, 63.24; H, 4.41; N, 14.74.

Treatment of **11** with Trifluoroacetic Acid.

A 6.00-g. (19.3 mmoles) quantity of Schiff base **11** in 25 ml. of trifluoroacetic acid was heated at reflux for 15 hours. Tlc indicated the absence of **11**. The solution was evaporated to dryness and the residue was triturated with ether. The resulting yellow solid was collected to yield 400 mg. of 9(10*H*)acridone (**18**), m.p. 357-359° dec., [lit. (12) m.p. 354°]; ir (Nujol): 3300-3150 (NH and CH), 1635 (C=O) cm^{-1}; nmr (trifluoroacetic acid): δ 8.90-7.60 (m); mass spectrum: (70 eV) m/e 195 (molecular ion). The infrared spectrum of **18** was identical to that recorded for an authentic sample (13). A mixture melting point of **18** with an authentic sample (14) was undepressed.

Anal. Calcd. for $C_{26}H_{18}N_2O_2$: C, 79.98; H, 4.65; N, 7.17. Found: C, 79.70; H, 4.74; N, 7.35.

The filtrate yielded a precipitate weighing 1.35 g. A 500-mg. portion of this solid was dissolved in ethyl acetate, washed with saturated sodium bicarbonate, and applied to a thick layer chromatography plate (EM Reagents; Silica Gel 60 F-254; 20 x 20 cm; 0.25 mm thick). The plate was eluted twice with 95:5 (chloroform:methanol). The major band was removed, extracted with chloroform-methanol, and concentrated. The residue was recrystallized once from ethanol-ether to yield **19** as clear prisms, m.p. 164-166°; ir (chloroform): 3440 and 3320 (NH_2), 1660 (broad, C=O groups) cm^{-1}; nmr (deuteriochloroform): δ 7.67-7.03 (m, 9H, aromatic), 4.67 (very broad s, 2H, NH_2), 2.64 (s, 3H, NCH_3), 2.03 (s, 3H, CCH_3); mass spectrum (70 eV) m/e 283 (molecular ion).

Anal. Calcd. for $C_{16}H_{17}N_3O_2$: C, 67.82; H, 6.05; N, 14.83. Found: C, 68.10; H, 6.29; N, 14.59.

2-(Phenylamino)benzoic Acid 1-Methyl-2-acetylhydrazide (**23**).

To 4.00 g. (20.7 mmoles) of **10** and 2.73 g. (20.7 mmoles) of triethylamine in 50 ml. of methylene chloride was added 1.62 g. (20.7 mmoles) of acetyl chloride. After stirring overnight, the reaction mixture was partitioned between water and methylene chloride. The organic layer was dried (sodium sulfate) and concentrated to afford 5.86 g. (quantitative yield) of **23** as a viscous oil; ir (Nujol): 3250 (broad NH), 1675 (C=O), 1640 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 7.60-6.57 (m, 9H, aromatic), 5.27 (broad s, 2H, both NH groups), 3.17 (s, 3H, NCH_3), 1.85 (s, 3H, $COCH_3$); mass spectrum: (70 eV) m/e 283 (molecular ion).

Methyl 2-(Acetylphenylamino)benzoate (**25**).

An 11.4-g. (50.0 mmoles) quantity of **24** and 8.64 g. (110 mmoles) of acetyl chloride in 50 ml. of toluene were heated at reflux for 15 hours, after which time **24** was absent by tlc. The reaction solution was concentrated to a viscous oil which was triturated with ether to produce a tan solid. The solid was collected, washed with ether and air-dried to yield 12.2 g. (91%) of **25**, m.p. 95-97°, m.p. 95.5-96.5° (ethanol-water); ir (Nujol): 1710 (ester C=O), 1655 (amide C=O) cm^{-1}; nmr (deuteriochloroform): δ 8.05-7.85 (m, 1H, H *ortho* to C=O), 7.60-7.00 (m, 8H, remaining aromatic), 3.86 (s, 3H, OCH_3), 2.05 (s, 3H, $COCH_3$).

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.50; H, 5.46; N, 5.33.

2-(Acetylphenylamino)benzoic Acid (**26**).

To a solution of 55.9 g. (0.208 mole) of **25** in 300 ml. of dimethoxyethane was added 96 ml. (0.240 mole) of 10% sodium hydroxide solution. The two-phase mixture was heated at reflux for 24 hours and the resulting clear solution was concentrated to remove most of the dimethoxyethane. The concentrated solution was diluted with 500 ml. of water and acidified with concentrated hydrochloric acid. The resulting precipitate was collected and air-dried to yield 50.6 g. (95%) of **26**, m.p. 143-144.5°, m.p. 144-145° (benzene-hexane); ir (Nujol): 3400-2200 (OH), 1695 (acid C=O), 1670 (amide C=O) cm^{-1}; nmr (deuteriochloroform): δ 11.88 (s, 1H, CO_2H, deuterium oxide exchangeable), 8.13-7.94 (m, 1H, H *ortho* to C=O), 7.60-7.05 (m, 8H, remaining aromatic), 2.08 (s, 3H, CH_3).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.50; H, 5.16; N, 5.49.

Preparation of **19** from **26**.

A 2.55-g. (10.0 mmoles) quantity of **26** was added to a solution of 1.40 g. (11.0 mmoles) of oxalyl chloride (Aldrich) in 40 ml. of benzene and stirred for 20 minutes. A yellow, gummy material was present as a precipitate, whose ir (neat) showed C=O bands at 1790 and 1715 cm^{-1}. The supernatant was decanted and the precipitated material was washed with benzene, dissolved in methylene chloride, and treated with excess methylhydrazine. After 15 hours the solution was washed with water, dried (sodium sulfate) and concentrated to yield 1.08 g. of oil. This material showed several spots on tlc, one of which corresponded to **19**. A 150 mg. portion of the oil was dissolved in methylene chloride and applied to a thick layer chromatography plate (EM Reagents; Silica Gel 60 F-254; 20 x 20 cm; 0.25 mm thick) and eluted four times with 93:7 (methylene chloride:methanol). The band corresponding to **19** was removed and extracted wtih methylene chloride-methanol to yield, after concentration, 30 mg. of amorphous solid. This material was indistinguishable from **19** by tlc, and an infrared spectrum (chloroform) of this material was identical to that of **19**.

Acknowledgment.

We thank E. Herman and J. Anderson for gathering much of the spectral data.

REFERENCES AND NOTES

(1) "The Benzodiazepines," S. Gralttini, E. Mussini, and L. O. Randall, Eds., Raven Press, New York, NY, 1973.

(2) N. P. Peet and S. Sunder, *J. Org. Chem.*, **40**, 1909 (1975).

(3) S. Sunder, N. P. Peet, and D. L. Trepanier, *ibid.*, in press.

(4) A. A. Santilli and T. S. Osdene, U. S. Patent 3,452,037 (1969); *Chem. Abstr.*, **71**, 81338g (1969).

(5) F. E. Condon, *J. Org. Chem.*, **37**, 3608 (1972).

(6a) O. M. Cherntsov, *J. Gen. Chem. (USSR)*, **14**, 186 (1944); *Chem. Abstr.*, **39**, 2291[2] (1945); (b) C. D. Hurd and O. E. Fancher, *J. Am. Chem. Soc.*, **69**, 716 (1947).

(7) A. M. Grigorovskii, *Zh. Obshch. Khim. (J. Gen. Chem., USSR)*, **19**, 1744 (1949); *Chem. Abstr.*, **44**, 2953d (1950).

(8) N. S. Drozdov, *J. Gen. Chem. (USSR)*, **8**, 937 (1938); *Chem. Abstr.*, **33**, 1330[6] (1939).

(9) 9(10*H*)Acridone (**18**) was also produced when Schiff base **11** was treated with polyphosphoric acid followed by an aqueous work-up. Hydrazide **10** was a coproduct of this reaction.

(10) H. Gilman, D. A. Shirley and P. R. Van Ess, *J. Am. Chem. Soc.*, **66**, 625 (1944).

(11a) M. Goodman, N. Arbiter and G. Powell, *ibid.*, 55, 4294 (1933); (b) D. Craig, *ibid.*, 57, 195 (1935).

(12) C. F. H. Allen and G. H. W. McKee, *Organic Synthesis, Coll. Vol.* **2**, 15 (1943).

(13) The infrared spectrum of **18** was identical to that reported for 9(10*H*)acridone by C. J. Pouchert, "The Aldrich Library of Infrared Spectra," Second Edition, 1975, spectrum 791C.

(14) An authentic sample of **18** was generated in our laboratory as a coproduct in the preparation of 2-(phenylamino)benzoyl chloride (8).