$HCCl_3$ and aqueous sodium carbonate. The residue of crude **6**, mp 50–53°, obtained from the separated, dried organic layer amounted to 0.1 g (51%). A sample purified by sublimation at 50° (0.05 mm) had mp 55–57°; pmr (CCl_4) 7.2 (t, 2, J = 6.5 Hz, CHNCH), 6.9 (s, 3, OCH_3), 6.58 (t, 2, J = 6.5 Hz, CHNCH), 6.1 (p, 1, J = 6 Hz, CHOMe), and 2.77 (m, 10, ArH).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.47; H, 7.69; N, 5.39.

1-Benzhydryl-3-ethoxyazetidine (**7**).—From 0.317 g (1 mmol) of **5**, 2 ml of absolute methanol, and 0.2 g of anhydrous sodium carbonate treated as described for the preparation of **6** was obtained 0.1 g (37%) of **7**, mp 65–67°, after sublimation of the crude product at 60° (1 mm): pmr (CCl_4) 8.93 (t, 3, J = 7.5 Hz, CH_2CH_3), 7.22 (t, 2, J = 7 Hz, CHNCH), 6.73 (q, 2, J = 7.5 Hz, CH_2CH_3), 6.58 (t, 2, J = 7 Hz, CHNCH), 6.0 (p, 1, J = 6 Hz, CHOEt), 5.73 (s, 1, Ph_2CH), and 2.75 (m, 10, ArH); molecular ion at m/e 267.259 (calcd for $C_{11}H_{21}NO$: 267.1623).

1-Benzhydryl-3-bromoazetidine (**8**).—1-Benzhydryl-3-methanesulfonatoazetidine (**5**) (12.7 g, 40 mmol) was added to a solution of 6.2 g (60 mmol) of NaBr in 80 ml of diethylene glycol. The mixture was heated at 60–65° for 2.5 hr, cooled to room temperature, and extracted with CCl_4. Removal of the solvent from the combined washed (H_2O) and dried extracts left 10.3 g (85%) of **8**, mp 95–99°. A sample recrystallized from ethanol had mp 101–102°; pmr (CCl_4) 6.65 (t, 2, J = 7 Hz, CHNCH), 6.31 (t, 2, J = 7 Hz, CHNCH), 5.65 (m, 1, CHBr), 5.61 (s, 1, Ph_2CH), and 2.67 (10, m, ArH).

Anal. Calcd for $C_{16}H_{16}NBr$: C, 63.59; H, 5.34; Br, 26.44; N, 4.65. Found: C, 63.71; H, 5.47; Br, 26.43; N, 4.77.

3,3′-Bis-1-benzhydrylazetidine (**9**).—A solution of 3.02 g (10 mmol) of **8** in 30 ml of dry ether was stirred under reflux with 0.243 g (10 g-atoms) of Mg turnings until the Mg disappeared (10 hr). Stirring was continued while gaseous CO_2 was passed over the solution for 2 hr. The mixture was poured onto crushed, solid CO_2 and the whole was extracted with H_2O. No precipitate formed when the separated aqueous phase was brought to pH 5 with 6 N hydrochloric acid. Removal of the solvent from the dried ether layer and chromatography [tlc on silica gel with 4:1 petroleum ether (bp 30–60°)–ether] of the residue gave unchanged **8** (R_f 0.9) and a small amount of **9** (R_f 0.75): mp 176°; pmr ($CDCl_3$) τ 7.28 (m, 6, 2 CHNCHCH), 6.84 (m, 4, 2 CHNCH), 5.76 (s, 2, 2 Ph_2CH), and 2.73 (m, 20, 2 ArH); molecular ion at m/e 444.257 (calcd 444.2565).

Anal. Calcd for $C_{32}H_{32}N_2$: C, 86.44; H, 7.26; N, 6.30. Found: C, 86.26; H, 7.38; N, 6.34.

1-Benzhydryl-3-cyanoazetidine (**10**).—To a solution of 95.1 g (0.3 mol) of **5** in 600 ml of DMF was added a solution of 44.1 g (0.9 mol) of NaCN in 75 ml of H_2O. The mixture was heated at 65° with stirring for 24 hr, cooled, and poured into an ice–water mixture. The precipitate was collected and dissolved in 400 ml of dichloromethane. Filtration of the dried organic solution through tlc grade silica gel removed colored impurities. Evaporation of the solvent gave 55.3 g (75%) of **10**: mp 152–153°; ir ($HCCl_3$) 2260 cm^{-1} (C≡N); pmr (CCl_4) τ 6.75 (m, 5, CH_2-$CHCH_2$), 5.7 (s, 1, Ph_2CH), and 2.7 (m, 10, ArH).

Anal. Calcd for $C_{17}H_{16}N_2$: C, 82.23; H, 6.45; N, 11.25. Found: C, 82.16; H, 6.41; N, 11.45.

1-Benzhydrylazetidine-3-carboxylic Acid (**11**).—Solutions of 9.9 g (40 mmol) of **10** in 100 ml of monoethoxyethanol and 8.08 g (144 mmol) of KOH in 6 ml of H_2O were combined and heated at 90–95° for 24 hr, at which time NH_3 evolution had ceased. The cooled solution was poured into an ice–water mixture and the whole was acidified (*ca.* pH 5) with 6 N hydrochloric acid. The precipitate after collection and drying amounted to 9.2 g (86%) of **11**, mp 180–190°. A sample after sublimation at 80° (10^{-3} mm) had mp 198°; ir (KBr) 1670 and 1370 cm^{-1} (C=O); pmr (DMSO-d_6) τ 6.7 (m, 5, CH_2CHCH_2), 5.54 (s, 1, Ph_2CH), 4.2 (broad s, 1, ^+NH), and 2.64 (m, 10, ArH).

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.37; H, 6.36; N, 5.24. Found: C, 76.34; H, 6.56; N, 5.36.

Reduction of 1-Benzhydryl-3-cyanoazetidine (**10**). **A. Catalytic.**—A mixture of the hydrochloride of **10** (2.85 g, 10 mmol) dissolved in 200 ml of dry methanol and 0.32 g of $Pd(OH)_2 \cdot C^{10}$ was treated with H_2 at room temperature and *ca.* 60 psi until about 0.01 mol of H_2 was taken up. The mixture was filtered, the solvent was evaporated from the filtrate, and the residue was extracted with dry THF. Examination (pmr, tlc) of the residue (1.5 g) from the THF extract indicated it to contain **10** plus a small amount of diphenylmethane. The insoluble residue (1.5 g) was partitioned between 6 N NaOH and $HCCl_3$. The spectra of the solid obtained from the dried organic layer indicated it to be impure **12**: ir ($CHCl_3$) 3300 cm^{-1} (NH); pmr ($CDCl_3$) τ 8.83 (s, 2, NH_2), 7.58 (m, 1, $CHCH_2N$), 7.23 [m, 4, $(CH)_2CCH_2N$], 6.8 (t, 3, J = 7 Hz, CHCCH), 5.77 (s, 1, Ph_2CH), 2.77 (m, 10, ArH); pmr [$CDCl_3$, *ca.* 0.05 M Eu(fod)$_3$][16] 7.03 (m, 1, $CHCH_2N$), 6.8 (t, 2, J = 7 Hz, CHCCH), 6.5 (t, 2, J = 7 Hz, CHCCH), 6.13 (d, 2, J = 7 Hz, $CHCH_2N$), 5.57 (s, 1, Ph_2CH), 4.37 (s, 2, NH_2), and 2.67 (m, 10, ArH); molecular ion at m/e 251.158 [calcd for $C_{17}H_{19}N_2$ (M − 1), 251.1548].

B. With Lithium Aluminum Hydride.—A solution of 2.48 g (10 mmol) of **10** in 30 ml of dry THF was added slowly to a suspension of 1.4 g (35 mmol) of lithium aluminum hydride in 10 ml of dry THF and the mixture was stirred overnight and then refluxed for 3 hr. Excess hydride reagent was hydrolyzed by the careful addition, with cooling, of saturated aqueous ammonium chloride, the gelatinous mixture was filtered and the filter cake was washed repeatedly with THF. Evaporation of the solvent from the combined, washed (saturated aqueous NaCl), and dried filtrates left a viscous, yellow oil which gave, after molecular distillation (*ca.* 0.01 mm), 1.79 g (72%) of material identical (ir, pmr and tlc) with the product from A.

3-Methanesulfonatoazetidinium Chloride (**13**).—A solution of the hydrochloride salt (3.54 g, 10 mmol) of the mesylate derivative **5** in 75 ml of absolute methanol was treated with H_2 in the presence of 0.32 g of $Pd(OH)_2 \cdot C^{10}$ at 50 psi until H_2 uptake ceased (1 hr). The mixture was filtered, the solvent was evaporated from the filtrate, and the solid residue was extracted with benzene. From the benzene extract was obtained 1.69 g of diphenylmethane. The residual solid was washed with dichloromethane and then amounted to 1.94 g (104%) of impure **13**, mp 99–101°. A sample after recrystallization from absolute ethanol had mp 104–105°; pmr (D_2O) τ 7.20 (s, 3, SCH_3), 5.97 (m, 6, H_2O, H_2CNCH_2), 4.97 (p, 1, J = 6 Hz, CHOMs).

Anal. Calcd for $C_4H_{10}NO_3ClS$: 3, 25.61; H, 5.34; Cl, 18.95; N, 7.46; S, 17.07. Found: C, 25.43; H, 5.43; Cl, 18.80; N, 7.60; S, 16.98.

Azetidine-3-carboxylic Acid (**2**).—A solution of 1 g (3.74 mmol) of the N-benzhydryl acid **11** in 200 ml of absolute methanol was treated with H_2 for 2 hr as described for the preparation of **13**. The initial solid residue was washed with ether and then amounted to 0.37 g (99%) of **2**. Paper (Whatman No. 3) chromatography (12:3:5 butanol–acetic acid–H_2O) gave a spot at R_f 0.32[17] which became purple when sprayed with ninhydrin. The material gave an intense blue color with Feigl's test for imino compounds. Electrophoresis showed migration toward the positive electrode. A sample recrystallized from 90% ethanol had mp 230–275° dec: ir (KBr) 2700–2400 ($^+NH_2$), 1620–1550, and 1400 cm^{-1} (CO_2^-); pmr (H_2O) τ 6.47 (m, 1, CH_2CHCH_2), 5.87 (d, 4, J = 7 Hz, CH_2CCH_2), and 5.3 (s, 2, H_2O); mass spectrum m/e 101.0477 (calcd 101.0477); pK_a^1 = 3.2 ± 0.1 and pK_a^2 = 10.3 ± 0.1.

Anal. Calcd for $C_4H_7NO_2$: C, 47.52; H, 6.93; N, 13.87. Found: C, 47.41; H, 6.94; N, 13.85.

Registry No.—**2**, 36476-78-5; **3**, 18621-17-5; **4**, 36476-80-9; **5**, 33301-41-6; **6**, 36476-82-1; **7**, 36476-83-2; **8**, 36476-84-3; **9**, 36476-85-4; **10**, 36476-86-5; **11**, 36476-87-6; **12**, 36476-88-7; **13**, 36476-89-8.

(16) Norell Chemical Co., Inc.

(17) The R_f values for proline and azetidine-2-carboxylic acid are 0.39 and 0.35, respectively, under these conditions.

Synthesis of 2-Benzazepine-1,3-diones and Corresponding 4,5-Dihydro Compounds

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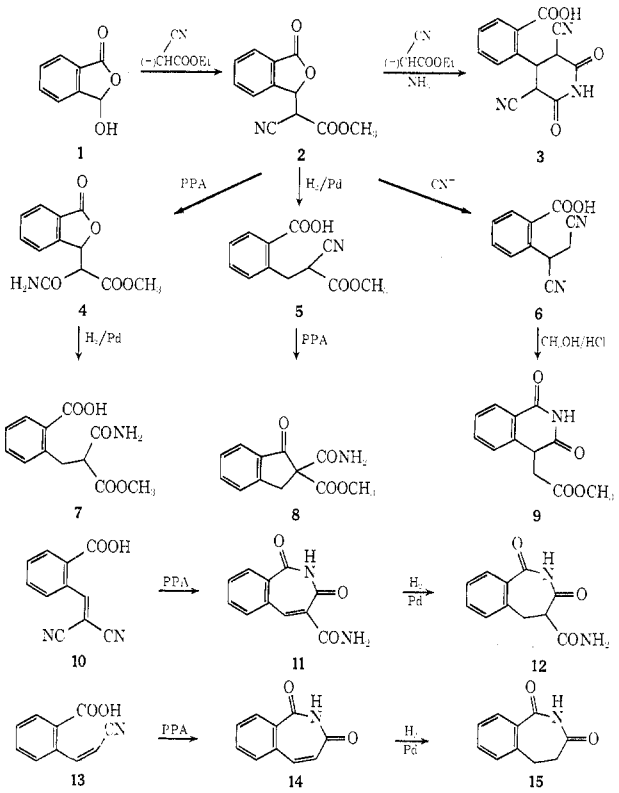
Earlier we reported on the PPA closure of α′-cyano-*trans*-stilbene-*o*-carboxylic acids and *o*-(2-cyano-2-phenylethyl)benzoic acids to 4-aryl-2-benzazepine-1,3-di-

ones and corresponding 4,5-dihydro-4-aryl-2-benzazepine-1,3-diones, respectively.[1] Syntheses of parent substances lacking the 4-aryl groups by a similar approach were also sought, and are now reported.

Consensation of the masked aldehyde group of phthalaldehydic acid (**1**)[2] (Scheme I) with reactive

SCHEME I



methylene group containing compounds[3] is quite facile in comparison with, *e.g.*, parallel reactions of *o*-benzoylbenzoic acid.[4] Reaction of **1** with ethyl cyanoacetate is even more rapid than that with phenylacetonitrile,[1] and the anion first formed may readily undergo further reactions with nucleophiles. Thus when an additional mole of ethyl cyanoacetate was added and the reaction solution was treated with NH_3, the Guareschi imide **3** was obtained.[5] Addition of (aqueous) cyanide after the initial reaction with ethyl cyanoacetate gave dinitrile **6**, which was characterized by conversion to the corresponding triacid and to homophthalimide ester **9**.

Acidification of a water solution of the sodium salt resulting from reaction of **1** with 1 equiv of sodio ethyl cyanoacetate gave nitrile ester lactone **2**. Attempts to obtain the carbomethoxy cinnamonitrile-*o*-carboxylic acid from the rather sensitive compound **2** by acid hydrolyses were unpromising. Treatment of **2** with PPA resulted merely in conversion of the nitrile group to the corresponding amide, **4**. The lactone moiety in this instance thus will not serve in the same capacity as an *o*-COOH group to attack the CN and produce an imide.[1] Alternatively, we investigated the possibility of PPA closure of hydrocinnamonitrile or amide *o*-carboxylic acids derived by ring opening of the lactones. Hydrogenolysis of **2** and **4** in the presence of Pd/C under mild conditions[6] did indeed give the benzoic acids **5** and **7**, respectively. However, no cyclic imides could be obtained by action of PPA on these compounds. The reason was apparent when it was ascertained that the PPA cyclization product from **5** was indanone **8**, acylation of the reactive methine rather than attack on the nitrile moiety having occurred, as in similar closure of benzoic acid 2-thioacetamides with Ac_2O–base to thianaphthenones.[7]

A crude, bicarbonate-soluble substance, which appeared to be mainly **10**, was prepared by condensation of **1** with 1 equiv of sodio malononitrile in methanol under mild conditions (as in **1** → **2**). PPA cyclization of the crude condensation product was more rapid than closures of other cinnamonitrile-*o*-carboxylic acids,[1] and from the bicarbonate-insoluble fraction of crude product there was isolated 2-benzazepine-1,3-dione-4-carboxamide (**11**) in low yield. Spectra agreed with structure **11**, and further confirmation was obtained by Pd hydrogenation of **11** to **12**, as in similar hydrogenation of the 4,5 double bond in our earlier 4-aryl analogs of **11**.[1]

To achieve a synthesis of 2-benzazepine-1,3-dione (**14**) itself, which appears to have been approached closely[8] but to date not reported specifically, hydrolysis and decarboxylation of **11** or **12** would not serve, and it was necessary to prepare *cis*-cinnamonitrile-*o*-carboxylic acid (**13**) by the reported inverse Beckmann rearrangement of β-nitroso-α-naphthol.[9] Treatment of **13** with PPA gave **14**, which interestingly showed long-range nmr coupling of vinyl proton 4 to imide proton 2 (see Experimental Section), and finally Pd hydrogenation of **14** afforded **15**.

Experimental Section[10]

Methyl α-(3-Phthalidyl)cyanoacetate (2).—To a solution of 9.3 g (0.405 g-atom) of Na in methanol (500 ml) was added 47 g (0.415 mol) of ethyl cyanoacetate (noticeably endothermic reaction), and 5 min thereafter 60 g (0.40 mol) of phthalaldehydic acid was added. The solution was warmed on a steam cone for 10 min, allowed to stand 0.5 hr while cooling slowly, and reheated on a steam cone for *ca.* 5 min. On standing the solution deposited a sodium salt in quantity. An aqueous solution of this salt was acidified (cooling) weakly with dilute HCl, and the product was collected, washed with water, pressed dry, and triturated with methanol to give 80 g (86%) of crystals, mp 132–134°. Recrystallization from methanol gave a pure sample: mp 140–141°; ir 4.44 (very weak) and 5.67–5.71 μ (doublet); uv 222 nm (ε 11,870) and 290 (9440) with inflection at 281 (9260).

Anal. Calcd for $C_{12}H_9NO_4$: C, 62.34; H, 3.92; N, 6.06. Found: C, 62.01; H, 3.82; N, 5.88.

Guareschi Imide (3).—To a solution of 2.6 g of Na in methanol was added 12 g of ethyl cyanoacetate and then 16.8 g of phthalal-

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(9) J. A. Elvidge and D. E. H. Jones, *J. Chem. Soc. C*, 2059 (1967), and discussion of earlier work therein.
(10) Melting points were obtained using a Thomas-Hoover silicone oil bath; ir spectra (Nujol mulls for solids, films or $CHCl_3$ solutions for oils) were taken on a Perkin-Elmer 21 double beam instrument; uv curves (MeOH solutions) were measured with a Cary 14 recording spectrophotometer; nmr spectra were obtained using a Varian A-60 apparatus, TMS internal standard. We are indebted to Mr. George Robertson and Mr. Rudolf Oeckinghaus for microanalyses, to Miss Ruth Behnke, Miss Natalie Cahoon, Mr. Mike Hotolski, Mr. Charles Navarro, and Mr. Anis Hamden of the staff of Mr. Louis Dorfman for spectral data, and to Mrs. Angela Aretakis for literature search work.

dehydic acid (1) which dissolved readily (mild exothermic effect). After *ca.* 5 min, additional ethyl cyanoacetate (12 g) was added. A stream of anhydrous NH_3 was passed into the solution without cooling, resulting in an exothermic effect and separation of white crystals. After the suspension had been allowed to stand overnight, the solid salt was collected, washed with methanol, and dissolved in water and the solution was acidified with dilute HCl. On standing there appeared a mass of crystals which were collected (two crops), washed with water sparingly, and dried: yield 22.9 g (76%); mp 185–187° dec (discolor from 175°), not raised on recrystallization from methanol; ir 3.12 (int, broad), 4.41 (weak), and 5.73–5.85 μ; uv 220–227 nm (ϵ 8760) and 274 (1510).

Anal. Calcd for $C_{14}H_9N_3O_4$: C, 59.36; H, 3.20; N, 14.84. Found: C, 59.02; H, 2.99; N, 14.68.

o-(1,2-Dicyanoethyl)benzoic Acid (6).—Reaction of 3.0 g of Na in 180 ml of methanol, 14 ml of ethyl cyanoacetate, and 18.4 g of **1** was carried out as described for **2**, after which a solution of 6.8 g of NaCN in 40 ml of water was added, resulting in dissolution of the sodium salt which had separated. The solution was boiled for 3.5 hr on a steam cone, allowing most of the methanol to escape. The cooled, diluted (water) solution on acidification effervesced and an oil separated; an ether extract of the oil was washed with water, dried ($MgSO_4$), and evaporated. The residue crystallized slowly in the presence of ether, giving on trituration with this solvent 7 g of crystals: mp *ca.* 165–166° dec (sinter from 120°) after recrystallization from ether; ir 4.43 and 5.90 μ; uv 227 nm (ϵ 8730) and 274 (1270) with inflection at 282 (1060). The compound was unstable, the crystalline material becoming sticky on standing.

Anal. Calcd for $C_{11}H_8N_2O_2$: C, 65.99; H, 4.03; N, 13.99. Found: C, 66.25; H, 4.18; N, 13.86.

The tricarboxylic acid corresponding to **6** was obtained by heating a sample of **6** with 20 parts of concentrated HCl on a steam code for 3 hr (excess reagent was evaporated); an ethyl acetate extract was dried ($MgSO_4$) and evaporated and the residue was triturated with ether and recrystallized from ethyl acetate: colorless crystals; mp 190–192° dec; ir 5.81–5.92 μ and broad OH and zwitterion bands; uv 226 nm (ϵ 7360) and 276 (1140).

Anal. Calcd for $C_{11}H_{10}O_6$: C, 55.46; H, 4.23. Found: C, 55.21; H, 4.12.

Homophthalimide **9** was obtained when a sample of **6** was refluxed for 3.5 hr with 50–100 parts of saturated methanolic HCl, the excess reagent was evaporated, the residue was treated with water, and the resulting crude crystals were recrystallized from ether: mp 185.5–187°; ir 5.80, 5.92, and 6.24 μ, and bonded NH band; uv 239 nm (ϵ 10,890), 280–285 (1407), 290 (1470), and 300–308 (980).

Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.92; H, 4.58; N, 6.23.

α-Carbomethoxy-α-3-phthalidylacetamide (4).—Cyano ester **2** (21 g) on mixing with PPA (88 g) gave a solution slowly, with moderate exothermic effect (temperature rise to 60°). The solution was heated at 100° with stirring for 1 hr. Hydrolysis of the cooled PPA solution with 700 ml of ice water gave colorless crystals which were collected, washed with water, and dried, yield 17 g. Trituration with methanol and recrystallization from ethyl acetate afforded crystals: mp 198–200°; ir 2.98, 3.14, 5.71–5.76 (doublet), and 5.97 μ; uv 228 nm (ϵ 9020), 273 (2570), and 280 (2570). The compound dissolved rather readily in dilute NaOH solution but not in $NaHCO_3$ solution. The amide ester lactone resisted further treatment with PPA.

Anal. Calcd for $C_{12}H_{11}NO_5$: C, 57.83; H, 4.45; N, 5.62. Found: C, 57.80; H, 4.29; N, 5.49.

o-(2-Carbomethoxy-2-cyanoethyl)benzoic Acid (5).—Hydrogenation of 23.4 g of **2** in 250 ml of ethyl acetate in the presence of 6 g of 10% Pd/C at 45-lb gauge pressure (Parr apparatus; 4-l. reserve tank) resulted in a pressure drop of 8 lb in 17 min. At this point the solution was filtered and evaporated; the residue crystallized readily in the presence of ether, giving 17 g of triturated product. Recrystallization from ether gave colorless crystals: mp 126.5–128°; soluble in $NaHCO_3$ solution; ir 4.46, 5.77, and 5.95 μ; uv 228 nm (ϵ 8500) and 277 (1560) with inflection at 285 (1310).

Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 62.04; H, 4.92; N, 6.03.

o-(2-Carbamoyl-2-carbomethoxy)benzoic Acid (7).—Hydrogenation (45-lb gauge) of 10.1 g of **4** in 200 ml of ethyl acetate and 150 ml of ethanol in the presence of 3 g of 10% Pd/C at 65° for 3 hr, filtration, and evaporation of the solution gave 6.5 g of colorless crystals: mp 206–208°, raised on recrystallization (EtOAc) to mp 209–210°; soluble in $NaHCO_3$ solution (slowly); ir 5.75, 5.96, 6.07 and NH_2 bands (2.99, 3.18 μ); uv 228 nm (ϵ 7960) and 278 (1200).

Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.35; H, 5.24; N, 5.49.

2-Carbomethoxy-1-indanone-2-carboxamide (8).—A mixture of 6 g of acid nitrile ester **5** and 70 g of PPA was stirred and heated (steam cone) for 1 hr. After ice water hydrolysis of the cooled, bright red-orange (greenish fluorescent) PPA solution, the crude material was extracted with ethyl acetate–ether. The washed ($NaHCO_3$ solution, water) and dried ($MgSO_4$) organic solution gave bright orange, semisolid material. A methanol solution of the crude material was filtered to remove *ca.* 0.8 g of a crystalline, bright yellow by-product (mp 271–273° dec after recrystallization from methanol; ir 5.90–5.95, 6.12–6.18 μ; uv λ_{max} 266, 305, and 410 nm; M^+ 301 in mass spectrum) whose exact constitution was not established.

On evaporation of the MeOH solution, the main product **8** crystallized, and with the aid of ether there was isolated *ca.* 4 g as discolored crystals, mp 153–156°. Recrystallization from ethyl acetate gave colorless crystals: mp 158–160°; ir 2.95, 3.13, 5.72–5.82 (doublet), and 5.96 μ; uv 251 nm (ϵ 13,650) and 296 (2670); positive test (red precipitate) with 2,4-dinitrophenylhydrazine.

Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.90; H, 4.82; N, 6.01.

2-Benzazepine-1,3-dione-4-carboxamide (11). A. Condensation.—Condensation of sodiomalononitrile (prepared by adding 18.2 g of malononitrile to a solution of 6.3 g of Na in 250 ml of methanol) with **1** (40.5 g), as in the preparation of **2**, resulted in rapid dissolution of the phthalaldehydic acid as it was added. The bright yellow, methanol solution was warmed gently for 10 min on a steam cone, allowed to stand for 1 hr, and, since there was no separation of a sodium salt, the solution was evaporated while warming gently (15 min) to remove most of the methanol. On addition of water, a clear, yellow solution was obtained. This was chilled and acidified with dilute HCl. The resulting yellow oil was extracted with ether, and the washed (water) and dried ($MgSO_4$) ether solution was evaporated, giving *ca.* 30 g of yellow, viscous oil, hardening to a cake of sticky, yellow solid after several days, mp *ca.* 110–115°; trituration with ether–ethyl acetate gave material, mp *ca.* 143–149°, but no solvent suitable for recrystallization of the rather unstable material could be found. It was for the most part soluble in $NaHCO_3$, and ir (2.78–2.91, 3.10, 4.46, 5.80, and 5.97 μ) indicated structure **10**, admixed with corresponding lactone and possibly also corresponding amides; uv λ_{max} 214, 292 nm and high end absorption.

B. Cyclization.—Crude A product (18.5 g) and PPA (160 g) were stirred and heated for 5 min on a steam cone, which soon produced a bright red-orange solution (longer heating resulted in evident decomposition, with frothing, leading to a dark brown color). The PPA solution was allowed to stand for 1.5 hr while cooling gradually to room temperature, and then it was hydrolyzed with *ca.* 1 l. of ice and water. The resulting yellow solid was collected, washed with water, and triturated with $NaHCO_3$ solution, refiltered, washed again with water, and triturated with methanol (or acetone) to remove greenish-orange, oily impurities. There remained 3.6 g of yellow crystals, mp 240–250° dec (softening at 230°). Further trituration with methanol raised the melting point to 247–251°, and finally recrystallization from ethyl acetate gave a pure sample as nearly colorless crystals: mp 268–270° dec; ir 2.96, 3.15, 5.85–5.96, 6.07 μ; uv 225 nm (ϵ 29,000) and 310 (10,130); nmr (DMSO) δ 11.6 (s, 1, exchanges with D_2O, imide NH), 8.5–7.6 (m, 6, exchanges with 2 D_2O, ArH and $CONH_2$), 8.1 (s, 1, vinyl H).

Anal. Calcd for $C_{11}H_8N_2O_3$: C, 61.11; H, 3.73; N, 12.96. Found: C, 61.46; H, 3.84; N, 12.68.

The compound had a remarkably powerful sternutatory effect on its investigator.

4,5-Dihydro-2-benzazepine-1,3-dione-4-carboxamide (12).—A solution of 1.2 g of **11** in 300 ml of EtOAc containing 1.5 g of 10% Pd/C was shaken under H_2 (45 lb) at 70–75° for 2.5 hr. Filtration of the catalyst and evaporation of the solvent gave a quantitative yield of colorless crystals, mp 217–222°. Recrystallization from EtOAc afforded a pure sample: mp 219–221°; ir 2.91, 3.15, 3.25, 5.92–5.99, and 6.17–6.25 μ; uv 241 nm (ϵ 10,950) and 282 (1660); nmr (DMSO) δ 10.7 (s, 1, exchanges with D_2O, imide NH), 8.1–6.9 (m, 6, exchanges with 2 D_2O, ArH and

$CONH_2$), 3.72 (t, 1, J = 5 Hz, proton 4), and 3.3 (d, 2, J = 5 Hz, methylene).

Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.54; H, 4.62; N, 12.84; mol wt, 218.21. Found: C, 60.71; H, 4.39; N, 12.54; M^+, 218.

The compound did *not* induce sneezing.

2-Benzazepine-1,3-dione (14). A. *cis-o*-Carboxycinnamonitrile (13) was prepared, following literature procedure, by treating 21 g of 2-nitroso-1-naphthol in 1 l. of ligroin with 26 g of PCl_5, stirring for several hours while HCl was evolved copiously, allowing the mixture to stand for 3 days, and taking the crude solid into *ca.* 200 ml of 10% NaOH solution; acidification of the filtered solution with 15% HCl and recrystallization of the cyano acid from methanol gave crystals of **13**, mp 177–179° (lit.[9] mp 172°, 179°).

B. PPA Closure.—A suspension of 2 g of **13** in 42 g of PPA was heated in a steam cone and stirred for 0.5 hr. The purple-brown solution was cooled and hydrolyzed with cold water; the crude crystals were collected, washed with water, triturated with dilute $NaHCO_3$ solution, and again collected, washed with water, and dried. Recrystallization from ether, filtering the solution free of dark sediment, gave 0.5 g of crystals: mp 142–143°; ir 3.14–3.28 (bonded NH), and 6.03–6.06 μ, with shoulders at 5.90–5.95 μ; uv 224 nm (ϵ 31,980), 281 (8600), and 321 (3830), with inflections at 288 (8360) and 306 (5740); nmr ($CDCl_3$) δ 9.4 (m, 1, exchanges with D_2O, imide NH), 8.5 (m, 1, proton 9), 7.6 (m, 3, ArH), 7.16 (d, 1, J = 12.5 Hz, proton 5), and 6.4 [q, 1, J = 12.5 Hz, coupling to proton 5, J' = 2.5 Hz (long range coupling to imide NH, disappearing on D_2O exchange of NH), proton 4].

Anal. Calcd for $C_{10}H_7NO_2$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.49; H, 4.14; N, 8.03.

4,5-Dihydro-2-benzazepine-1,3-dione (15).—Hydrogenation of **14** as for **11** at 65° for 1.5–2 hr, and evaporation of the filtered, colorless solution, gave crystals, from ethyl acetate–ether: mp 118.5–120.5°; ir 3.11–3.25, 5.90, and 6.00 μ; uv 239 nm (ϵ 12,870) and 282 (1760); nmr ($CDCl_3$) δ 8.76 (m, 1, exchanges with D_2O, imide NH), 8.1 (m, 1, proton 9), 7.34 (m, 3, ArH), and 2.96 (resembling q, 4, J's not first order, methylenes).

Anal. Calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.22; H, 5.25; N, 7.93.

Registry No.—**2**, 36004-42-9; **3**, 36004-43-0; **4**, 36004-44-1; **5**, 36004-45-2; **6**, 36015-22-2; **6** (tricarboxylic acid derivative), 36004-46-3; **7**, 36004-47-4; **8**, 36004-48-5; **9**, 36004-49-6; **11**, 36004-50-9; **12**, 36004-51-0; **14**, 36004-52-1; **15**, 36004-53-2.

Synthesis of Some 7-Aryl-6-azapteridines from 1,2,4-Triazine Intermediates

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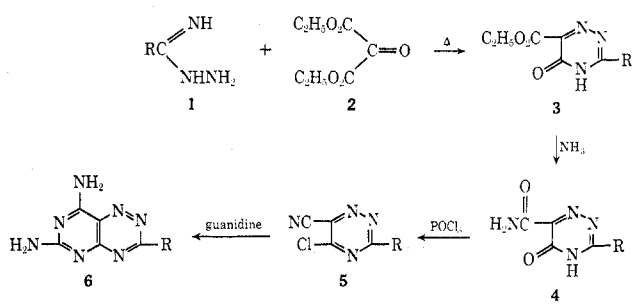
Interest in the pyrimido[4,5-*e*]-*as*-triazine (6-azapteridine) and pyrimido[5,4-*e*]-*as*-triazine (7-azapteridine) ring systems has intensified recently[2–7] as a consequence of the discovery that certain derivatives of the former ring system exhibit antiviral activity,[8] and that a number of broad-spectrum antibiotics (toxoflavin, fervenulin, and 2-methylfervenulone) are derivatives of the 7-azapteridine ring system.[9] We have explored the possibility of utilizing a common intermediate for the synthesis of both isomeric ring systems, and our results are summarized in this brief report.

The condensation of amidrazones with α,β-dicarbonyl compounds to give *as*-triazines is well known,[10–12] but none of the many *as*-triazines thus far prepared by this route possesses substituent groups suitable for subsequent cyclization to an azapteridine. It occurred to us that the reaction of amidrazones (**1**) with diethyl oxomalonate (**2**) should afford *as*-triazines[13] (**3**) which could readily be converted into 6-azapteridines (**6**) by the sequence of reactions depicted in Scheme I.

SCHEME I



Indeed, this concept proved to be successful when R = aryl, but it failed at the dehydration–chlorination step (**4** → **5**) with R = alkyl (CH_3, C_2H_5). Many different reaction conditions were explored ($POCl_3$, $POCl_3$–pyridine, $POCl_3$–DMF, $SOCl_2$–pyridine, $SOCl_2$–DMF), but in all cases only resinous, uncharacterizable products were obtained.

There is little ambiguity as to the structure of the condensation products formed in the above reaction (see Scheme I), since the keto grouping of diethyl oxomalonate is considerably more reactive than the ester groups, and N^1 of the amidrazone[14] is the most nucleophilic nitrogen. However, the structural assignments were confirmed independently by the unequivocal synthesis of **3** (R = C_6H_5, CH_3) by the reaction of the hydrazone of diethyl oxomalonate (**8**)[15] with the imidate esters **7** (R = C_6H_5, CH_3) (see Scheme II). The products of this latter condensation were identical in every respect with the corresponding compounds prepared by the alternate procedure described in Scheme I.

In principle, protection of N^1 of the amidrazone fol-

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(13) This route to *as*-triazines is not new; diethyl oxomalonate and thiosemicarbazide, for example, are known to give **3**, R = SH [R. B. Barlow and A. D. Welch, *J. Amer. Chem. Soc.*, **78**, 1258 (1956)].

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