264°; $[\alpha]_D^{27}$ −26.0° (0.32% in 95% ethanol); $\lambda_{max(\mu)}^{Nujol}$ 2.93, 3.03, 3.14, 5.82, 6.12, 6.25 (guanine pattern); 5.70 (*O*-acetate), no *N*-acetate at 5.90 or 6.48; $\lambda_{max(m\mu)}^{pH\ 1}$ 257 (ε 12,400), 280 (ε 8,700); R_{Ad} 1.42, in solvent A.[25]

Anal. Calcd. for $C_{14}H_{17}N_5O_6 \cdot {}^1/_2H_2O$: C, 46.7; H, 5.01; N, 19.4. Found: C, 46.4; H, 5.00; N, 19.0.

A subsequent acetylation of 1.8 g. of 5′-deoxyguanosine (XI) gave after one recrystallization 1.9 g. (78%) of diacetate (XIII), m.p. 258–260°, that had an infrared spectrum very similar to that of the analytical sample and had identical paper chromatographic behavior.

2-Amino-9-(5′-deoxy-β-D-ribofuranosyl)-9-H-purine-6-thiol (III). A mixture of 550 mg. (1.53 mmoles) of 2′,3′-di-*O*-acetyl-5′-deoxyguanosine (XIII) and 1.25 g. (5.6 mmoles) of phosphorus pentasulfide was added to 33 ml. of dry pyridine. The reaction was heated to reflux and 82 λ of water were added dropwise from a microburette, giving a cloudy solution which was heated at reflux for 8 hr. with stirring under nitrogen atmosphere. After the addition of 50 ml. of water the mixture was heated on a steam bath for 2 min., then cooled and adjusted to *p*H 6 with saturated aqueous sodium bicarbonate.

Extraction of the aqueous solution with 20 ml. of chloroform caused the separation of a precipitate which remained suspended in the chloroform layer. The chloroform layer containing the precipitate was drawn off and the aqueous layer was extracted further with four additional 20-ml. portions of chloroform. The combined chloroform extracts and solid were concentrated to dryness *in vacuo* to yield 340 mg. of a red-brown solid (XII). Trituration of the crude blocked nucleoside (XII) with 10 ml. of chloroform gave 270 mg. (47%) of an off-white product (XII) m.p. 230–236°. Continuous extraction of the aqueous phase above for 6 hr. with chloroform gave an additional 47 mg. (total yield 55%) of white solid, m.p. 230–235°; $\lambda_{max(\mu)}^{Nujol}$ 5.71 (acetate C=O) 8.34 (>C=S); $\lambda_{max(m\mu)}^{pH\ 1}$ 344 (ε 18,700); R_{Ad} 1.62 in solvent A[25] with trace components at R_{Ad} 0.0 and 0.25.

A mixture of 270 mg. of the crude diacetate (XII) and 10 ml. of methanol was saturated with ammonia at 5–10°, causing complete solution. After 16 hr. at 5°, a small amount of insoluble residue was removed by filtration and the filtrate was concentrated to dryness *in vacuo* to give 225 mg. of brown solid which had $\lambda_{max(m\mu)}^{pH\ 13}$ 318 (ε 15,100). Pure 5′-deoxythioguanosine (III) had $\lambda_{max(m\mu)}^{pH\ 13}$ 318 (ε 19,000). Thus, crude III above contained 80% of III (thioguanyl moiety). The crude nucleoside (III) showed a major component at R_{Ad} 0.61 and 1.55 in solvents A and B,[25] respectively, along with minor amounts of contaminants.

Recrystallization from 25 ml. of water gave 115 mg. (32% based on XIII) of material, m.p. 241–246° dec. Further recrystallizations from water gave the analytical sample, m.p. 252–252.5° dec.; $[\alpha]_D^{28}$ −62° (0.5% in *N,N*-dimethylformamide); $\lambda_{max(m\mu)}^{Nujol}$ 3.01, 3.07, 3.16, 6.08, 6.23, 6.28 (thioguanine pattern); 8.31 (C=S); $\lambda_{max(m\mu)}^{pH\ 1}$ 264 (ε 7,700), 344 (ε 21,300); $\lambda_{max(m\mu)}^{pH\ 13}$ 252 (ε 12,900), 318 (ε 19,000)[29]; R_{Ad} 0.61 in solvent A and 1.55 in solvent B.

Anal. Calcd. for $C_{10}H_{13}N_5O_3S$: C, 42.4; H, 4.62; N, 24.7; S, 11.2. Found: C, 42.3; H, 5.51; N, 24.6; S, 11.3.

A second crop of 35 mg., m.p. 243–247° dec., was obtained on concentration of the mother liquors. The paper chromatograms of the second crop were essentially identical with that of the analytical sample with R_{Ad} 0.68 in solvent A and R_{Ad} 1.47 in solvent B.

Acknowledgment. The authors are indebted to Dr. Peter Lim and staff for the chromatograms, optical rotations, and interpretation of the infrared spectra, and to Mr. O. P. Crews, Jr., and his staff for the large-scale preparations of intermediates.

MENLO PARK, CALIF.

(29) Fox, *et al.*[8] reported $\lambda_{max(m\mu)}^{pH\ 4-6}$ 257 (ε 8820), 342 (ε 24,800); $\lambda_{max(m\mu)}^{pH\ 10-12}$ 252 (ε 14,700), 319 (ε 21,000) for thioguanosine.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

Substituted γ-Lactones. VI.[1] Synthesis of Certain *p*-Substituted α-Benzylidene- and α-Benzyl-γ-butyrolactones as Potential Anticancer Compounds

HANS ZIMMER[2] AND RALPH E. DEBRUNNER[3]

Received July 18, 1960

A series of *N*-substituted glycines and precursors has been prepared. These compounds are derivatives of α-(4-aminobenzylidene)- and α-(4-aminobenzyl)-γ-butyrolactone. They can be obtained best from the corresponding α-(4-aminobenzylidene)- or α-(4-aminobenzyl)-γ-butyrolactones. The chemistry of these compounds and their preparation is discussed.

In our investigation of substituted γ-butyrolactones we became interested in the chemistry and pharmacology of amines derived from α-benzylidene-γ-butyrolactone and α-benzyl-γ-butyrolactone, because it recently has been shown that certain unnatural amino acids and derivatives thereof have interesting properties as cancer chemotherapeutica.[4] It also has been known for sometime that various compounds structurally related to, but not identical with, essential amino acids exhibit antimetabolic character.[5] Zimmer and Rothe[6] have prepared α-(4-dimethylaminobenzyl-

(1) Paper V in this series: H. Zimmer, J. Rothe, and J. Holbert, *J. Org. Chem.*, **25**, 1234 (1960).

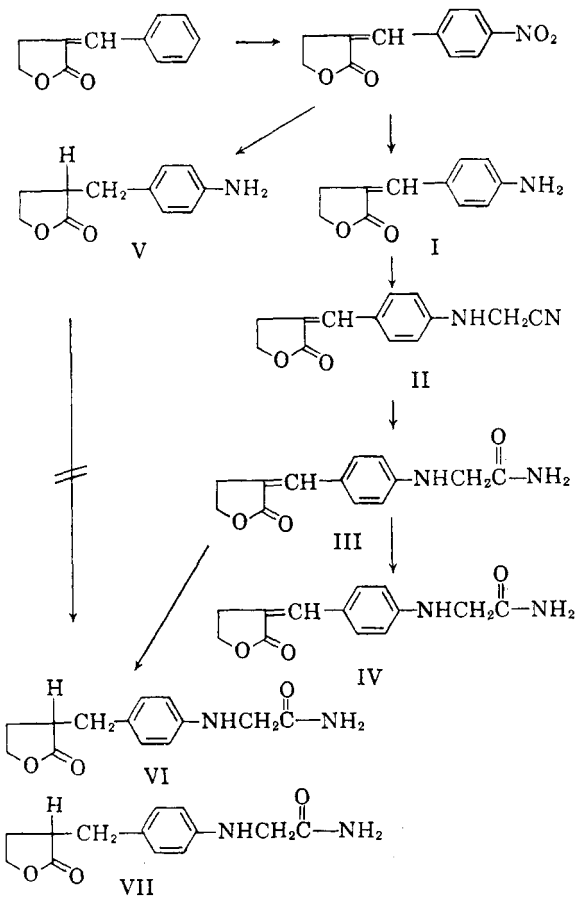
(2) Presented before the Division of Medicinal Chemistry, ACS Meeting, Cleveland, Ohio, April 11, 1960.

(3) Taken in part from Ph.D. thesis of R. E. DeBrunner, University of Cincinnati (1960), 1957–58, Procter and Gamble fellow, 1959, Chattanooga Medicine Company fellow.

(4) F. Bergel, J. M. Johnson, and J. A. Stock, *Chem. & Ind. (London)*, 1489 (1959).

idene)-γ-butyrolactone and preliminary testing shows favorable results in its use against cancer in mice. It seemed logical to follow up these findings and prepare amino acids containing the γ-lactone moiety. Our main work was therefore directed towards the synthesis of *N*-substituted amino acids and their precursors.

The synthesis of this type of compound proved to be more difficult than anticipated. As already reported in an earlier paper,[6] the condensation between γ-butyrolactone and negatively substituted benzaldehydes such as *p*-cyano- and *p*-nitrobenzaldehyde proceeds only in very small yields while the condensation with *p*-acetamidobenzaldehyde is only slightly better. The use of *p*-aminobenzaldehyde appeared to be unadvisable because of the highly basic conditions necessary for the condensation and the limited stability of the aldehyde under these conditions. Once a condensation was completed to give the substituted α-benzylidene-γ-butyrolactone, one was limited to neutral or acid conditions for any further reactions because of the sensitivity of the lactones to basic conditions. Therefore, the problem was approached by introducing the desired functional groups starting with the α-(4-nitrobenzylidene)-γ-butyrolactone which was prepared as reported earlier and which was reduced to the corresponding α-(4-aminobenzylidene)-γ-butyrolactone (I).[6]



The most obvious route for the preparation of the *N*-substituted glycine would be the condensation of I with chloroacetic acid, but all attempts of this resulted in oils and tars. Therefore another route to obtain the desired compounds was developed. The following chart illustrated the performed reactions and compounds obtained.

Cyanomethylation of I yielded α-(4-cyanomethylbenzylidene)-γ-butyrolactone (II), and hydrolysis of this nitrile gave the corresponding amide (III) and acid (IV). It was found that the success of the cyanomethylation depended very much on the solvent. Only if glacial acetic acid was used did the reaction proceed smoothly and in fairly good yields. Dioxane, dioxane-water, water, and ethanol-water as solvents did not give any of the desired product.

Treating II with concentrated sulfuric acid at room temperature gave III, while refluxing it with aqueous sulfuric acid gave the acid (IV). Both reactions proceeded to give satisfactory yields.

Application of the cyanomethylation reaction to α-(4-aminobenzyl)-γ-butyrolactone (V) always resulted in oils and tars which could not be induced to crystallize nor could they be purified by distillation without decomposition. Treating this oil with concentrated sulfuric acid gave another unidentified oil rather than the expected amide (VI). The amide (VI), however, was prepared by hydrogenation of III using platinum oxide as the catalyst. Raney nickel was not effective under the reaction conditions. Hydrolysis of VI by aqueous sulfuric acid gave the desired acid (VII).

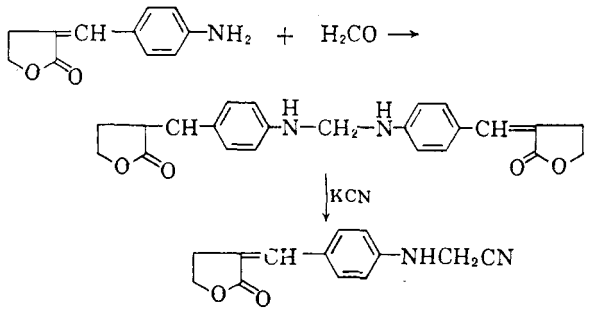
As expected, I is a rather weak base; however, it still could be diazotized to yield a normal diazonium compound which readily underwent a Sandmeyer reaction. It was further characterized by coupling with β-naphthol and *N*,*N*-dimethylaniline to the expected products. 2-[4-(*p*-Dimethylaminophenyl)azobenzylidene] - 4 - hydroxybutyric acid γ-lactone was obtained whereas the coupling with β-naphthol led to the free acid, 2-[4-(β-hydroxy-α-naphthyl)azobenzylidene] - 4 - hydroxybutyric acid, which could without difficulty be lactonized to the expected γ-lactone by refluxing the acid with acidic acetone.

In the cyanomethylation of I some interesting observations concerning the mechanism of this reaction were made. A solution of 37% aqueous formaldehyde was added to a solution of the amine in glacial acetic acid at room temperature. Immediately a precipitate formed. To this mixture was then added a potassium cyanide solution; after stirring for a time, a clear solution was ob-

(5) V. du Vigneaud, K. Dittmer, *J. Biol. Chem.*, **159**, 385 (1945); K. Dittmer, *J. Am. Chem. Soc.*, **71**, 1205 (1949); F. Dunn and K. Dittmer, *J. Biol. Chem.*, **188**, 262 (1951).

(6) H. Zimmer and J. Rothe, *J. Org. Chem.*, **24**, 28 (1959) and **24**, 100 (1959).

tained. The immediate formation of the precipitation upon the addition of formaldehyde indicated that the first step of the reaction was a condensation of the amine with formaldehyde. This condensation product was then attacked by the cyanide to give the desired product. The condensation product was isolated and found to be a yellow high-melting compound (259–260°). It was very insoluble in all commonly used solvents. Its infrared spectrum showed an NH-stretching band at 3.0μ besides peaks at 5.82μ and 6.1μ corresponding to a lactone carbonyl group and a C=C double bond. These observations, in addition to an elemental analysis which agreed reasonably well, suggested the structure of this condensation product to be methylene-*N*,*N*-bis[α-(4-aminobenzylidene)-γ-butyrolactone]: These findings agree with the original observations made by the inventors of this reaction, W. v. Miller and J. Plochl[7] and E. Knoevenagel.[8] They also agree with later observations by N. Drozdov[9] but do not agree with Bersworth and co-workers,[10] who reported that the first step in this reaction is a condensation between formaldehyde and cyanide to form a substituted ethylene oxide followed by a subsequent reaction with the amine.



The infrared spectrum of II is very interesting in that it showed no nitrile peak. Carbon-nitrogen triple bonds normally show a rather sharp stretching peak in the 4.2–4.5μ range.[11] Since numerous derivatives of this compound have been prepared there is no doubt that the assumed structure is correct. In the literature there are several examples of nitriles in which the expected carbon-nitrogen triple bond stretching peak is either greatly reduced or entirely absent. Bellamy[11] reported that the absence of absorption in the region cannot be taken as evidence for the absence of —C≡N groups, particularly if electronegative atoms such as oxygen are present in the position alpha to the cyano group.

(7) W. v. Miller and J. Plochl, *Chem. Ber.*, **25**, 2020 (1892).

(8) E. Knoevenagel, *Chem. Ber.*, **37**, 4081 (1904).

(9) N. Drozdov, *J. Gen. Chem. USSR*, **1**, 1171 (1931).

(10) R. Smith, J. Bullock, F. Bersworth, and A. Martell, *J. Org. Chem.*, **14**, 355 (1949); A. Martell and F. Bersworth, *J. Org. Chem.*, **15**, 46 (1950); L. Ziemlak, J. Bullock, F. Bersworth, and A. Martell, *J. Org. Chem.*, **15**, 225 (1950).

(11) L. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1954.

EXPERIMENTAL

The infrared spectra were obtained with a Baird double beam spectrophotometer using Nujol as a medium. Melting points are not corrected. Analysis by A. Bernhardt, Max Planck-Institute, Mülheim (Ruhr), Germany.

α-(4-Cyanomethylaminobenzylidene)-γ-butyrolactone (II). To a solution of 30.24 g. of α-(4-aminobenzylidene)-γ-butyrolactone[9] (0.16 mole) in 1600 ml. of glacial acetic acid was added 145.6 ml. of a 37% solution of formaldehyde (1.6 moles). The mixture was stirred thoroughly while a solution of 10.40 g. of potassium cyanide in 100 ml. of water was added dropwise. The addition required 0.5 hr. The reaction mixture was stirred vigorously at room temperature for 0.75 hr., then was heated until solution was complete (70°), and held at this temperature for 0.25 hr. An additional 20.80 g. of potassium cyanide was added in portions to the hot reaction mixture and the temperature was maintained at 75° for an additional 0.75 hr. before permitting the solution to cool. The acetic acid and water were distilled off under vacuum until the residue was about 350 ml. This residue was filtered and was diluted slowly with 2 l. of water with vigorous stirring. The resulting precipitate was collected by suction filtration, washed with water, and dried in a vacuum desiccator. The product was recrystallized from 3 l. of 95% ethanol giving 27.05 g. (74.1%) of product, m.p. 201–204°. After three recrystallizations from ethanol, the m.p. was 203–205°. This compound was identified by its hydrolysis to the corresponding acid amide and carboxylic acid. Infrared spectrum: 2.95 μ (NH amine); 5.75 μ (C=O, γ-lactone); 6.05 μ (C=C).

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 67.95; H, 5.65; N, 12.21.

α-(4-Carbamoylmethylaminobenzylidene)-γ-butyrolactone (III). To 360 ml. of concd. sulfuric acid at 0° was added 19.40 g. of α-(4-cyanomethylaminobenzylidene)-γ-butyrolactone (0.085 mole). The resulting red solution was permitted to stand at −10° for 108 hr., and then at room temperature for 20 hr. The solution was then poured onto 1500 g. of crushed ice with vigorous stirring. The resulting precipitate was removed by suction filtration and discarded. The filtrate was partially neutralized with 200 ml. of concd. aqueous ammonia while being stirred vigorously and cooled by an ice bath. The resulting precipitate was removed by filtration and discarded. Additional concd. aqueous ammonia was added to the filtrate until precipitation was complete. The precipitate was collected by filtration, washed thoroughly with water, and then dried in a vacuum desiccator to give 15.55 g. (71.6%) of yellow crystals, m.p. 232–234°. After three recrystallizations from 95% ethanol the m.p. was 236.5–237.5°. Infrared spectrum: 2.90 μ, 2.97 μ, 3.15 μ (NH, amine and amide); 5.83 μ (C=O, γ-lactone); 6.10 μ (C=C); 6.27 μ (C=O, amide).

Anal. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.12; H, 5.79; N, 11.26.

α-(4-Carboxymethylaminobenzylidene)-γ-butyrolactone (IV). A solution of 3.42 g. of α-(4-cyanomethylaminobenzylidene)-γ-butyrolactone (0.015 mole) in 300 ml. of 50 weight % sulfuric acid was refluxed for 2 hr. The color of the solution progressed from yellow to dark red during the time of heating. The reaction mixture was cooled and neutralized by dropwise addition of concd. aqueous ammonia, with stirring, until precipitation was complete. The precipitate was collected by suction filtration and dried to give 1.72 g. (46.4%) of a yellow product, m.p. 206° dec. This product was stirred with 200 ml. of water (*p*H 7–8) for 0.5 hr. and then filtered. The filtrate was extracted twice with ether, treated with charcoal, and then acidified with dilute hydrochloric acid until precipitation was complete. The precipitation was collected by suction, washed with water, and recrystallized

from 35% ethanol. The product was collected and dried to give 0.57 g. of yellow crystals, m.p. 210° dec. Infrared spectrum: 3.00 μ (amine); 3.7–4.0 μ (OH, acid); 5.79 μ (C=O, γ-lactone); 5.97 μ (C=O, acid); 6.13 μ (C=C).

Anal. Calcd. for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.57; H, 5.42; N, 5.66.

α-(4-Carbamoylmethylaminobenzyl)-γ-butyrolactone (VI). The hydrogenation of 3.69 g. of α-(4-carbamoylmethylaminobenzylidene)-γ-butyrolactone (0.015 mole) was accomplished by suspending the compound in 350 ml. of 95% ethanol and shaking under 50 lbs. of hydrogen in a Parr apparatus for 9 hr. The catalyst was 0.5 g. of platinum oxide. The catalyst was removed by filtration and the ethanol was removed by vacuum distillation until a residue of 50 ml. remained. Crystallization occurred after chilling the residue in an ice bath. The white crystals were collected and dried to give 1.68 g., m.p. 149–151°. A second crop of crystals gave 0.25 g., m.p. 145–148°. The total yield was 1.93 g. (51.9%). Three recrystallizations from ethanol gave a product, m.p. 152–154°. Infrared spectrum: 2.85 μ, 3.05 μ shoulder, 3.10 μ (NH, amine and amide); 5.55 μ (C=O, γ-lactone); 6.01 μ (C=O, amide).

Anal. Calcd. for $C_{13}H_{16}N_2O_3$:C, 62.89; H, 6.50; N, 11.28. Found: C, 62.93; H, 6.57; N, 11.55.

The same reaction was also attempted using 1–2 g. of Raney nickel as catalyst and dioxane as solvent. The product in this attempt was an oil which could not be worked up.

α-(4-Carboxymethylaminobenzyl)-γ-butyrolactone (VII). A solution of 1.86 g. of α-(4-carbamoylmethylaminobenzylidene)-γ-butyrolactone (0.0075 mole) in 15 ml. of 10% sulfuric acid was refluxed for 3.5 hr. The reaction solution was chilled to 0° and neutralized by dropwise addition of concd. aqueous ammonia. The tarry precipitate was separated and discarded. The filtrate was acidified to about *p*H 2 with cold concd. hydrochloric acid. The resulting precipitate was collected, washed with cold water and dried to give 0.60 (32.5%) of product, m.p. 127–130° dec. Recrystallizations from water and from isopropyl alcohol gave white crystals, m.p. 130–131°. Infrared spectrum: 2.97 μ (NH, amine); 3.8–4.3 μ band (OH, acid); 5.7–5.9 μ band (C=O, probably acid and lactone); 10.9–11.0 μ band (OH, acid).

Anal. Calcd. for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.75; H, 6.00; N, 5.60.

2-[4-(p-Dimethylaminophenyl)azobenzylidene]-4-hydroxybutyric acid, γ-lactone. A solution of 4.72 g. of α-(4-aminobenzylidene)-γ-butyrolactone (0.025 mole) in 15 ml. of concd. hydrochloric acid was chilled to 0°. A solution of 1.79 g. of sodium nitrite (0.026 mole) in 10 ml. of water was added with vigorous stirring to the cold solution of the amine hydrochloride; after this the solution gave a positive test with starch-iodide paper and with β-naphthol. The cold solution of the diazotized amine was added dropwise to an ice-cold, vigorously stirred solution of 2.67 g. of dimethylaniline (0.022 mole) in 20 ml. of 6*N* hydrochloric acid. When the addition was completed the mixture was stirred at −5° to 0° for 1 hr.; then, with continued stirring the mixture was permitted to warm to room temperature. When the mixture reached 20° it was neutralized with sodium bicarbonate (caution: foaming). The resulting precipitate was collected, washed with water, and dried in a desiccator over anhydrous calcium chloride to yield 3.40 g. (48.1%) of crude product, m.p. 220–230° dec. Recrystallization three times from acetone and twice from 95% ethanol gave an analytically pure sample of deep orange crystals, m.p. 251–252°. Infrared spectrum: 5.75 μ (C=O, lactone); 6.05 μ (C=C).

Anal. Calcd. for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 71.27; H, 6.00; N, 12.84.

2-[4-(β-Hydroxy-α-naphthyl)azobenzylidene]-4-hydroxybutyric acid. To an ice-cold solution of 4.73 g. of α-(4-aminobenzylidene)-γ-butyrolactone (0.025 mole) in 15 ml. of 6*N* hydrochloric acid was added with stirring a cold solution of 1.79 g. of sodium nitrite (0.026 mole) in 10 ml. of water. The cold solution of diazotized amine was added dropwise to an ice-cold, vigorously stirred solution of 3.17 g. of β-naphthol (0.022 mole) in 30 ml. of 6*N* sodium hydroxide. The temperature of the reaction was maintained at 0° during the addition of the diazotized amine and, with stirring continued, for 1 hr. after addition was complete. The reaction mixture was then acidified carefully with 25 ml. of 6*N* hydrochloric acid and then stirred for 1 hr.; the temperature during these operations was carefully maintained at 0°. The mixture was permitted to warm to room temperature, diluted with 150 ml. of water, and filtered and dried to give 6.3 g. (79%) of crude product, m.p. 230–237°. Several recrystallizations from acetone gave an analytical sample of deep purple crystals. Infrared spectrum: 3.02 μ (OH, alcohol); 3.85 μ (OH, acid); 5.95 μ (C=O, acid); 10.8 μ (OH, acid).

Anal. Calcd. for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.00; N, 7.73. Found: C, 69.53; H, 4.85; N, 7.85.

2-[4-(β-Hydroxy-α-naphthyl)azobenzylidene]-4-hydroxybutyric acid, γ-lactone. To a refluxing solution of 0.2 g. of 2-[4-(β-hydroxy-α-naphthyl)azobenzylidene]-4-hydroxybutyric acid (0.00055 mole) in 500 ml. of acetone was added 50 ml. of 1*N* sulfuric acid. The solution was refluxed for 0.5 hr. and then cooled to 0° for 72 hr. The resulting precipitate was collected and dried, giving 0.15 g. of a deep purple product, m.p. 242–247°. Two recrystallizations from acetone gave an analytical sample, m.p. 248–250°. A mixture m.p. with authentic starting material was 190–230°. Infrared spectrum: 5.75 μ (C=O, γ-lactone).

Anal. Calcd. for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.14. Found: C, 73.68; H, 4.42; N, 7.59.

Methylene-N,N-bis[α-(4-aminobenzylidene)-γ-butyrolactone]. To a solution of 3.02 g. of α-(4-aminobenzylidene)-γ-butyrolactone (0.016 mole) in 160 ml. of glacial acetic acid was added 14.6 ml. of a 37% aqueous solution of formaldehyde (4.80 g., 0.16 mole). After mixing for 1 hr. at room temperature the precipitate was collected, washed with water and dried to yield 2.86 g. of a product, m.p. 227–230°. Two recrystallizations from *N,N*-dimethylformamide gave a yellow product, m.p. 259–260°. (The compound was too insoluble to be recrystallized from any other solvent.) Infrared spectrum: 3.00 μ (NH, amine); 5.85 μ (C=O, γ-lactone; 6.10 μ (C=C).

Anal. Calcd. for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.18. Found: C, 69.94; H, 5.63; N, 7.54.

Acknowledgment. The authors acknowledge gratefully stimulating discussions with Dr. F. Haupter. A generous gift of α-(4-nitrobenzylidene)-α-butyrolactone from Chattem Chemicals, Chattanooga 9, Tenn., is greatly appreciated.

CINCINNATI 21, OHIO