Cyclization of Ylidenemalononitriles. V. Formation of Substituted γ-Lactones

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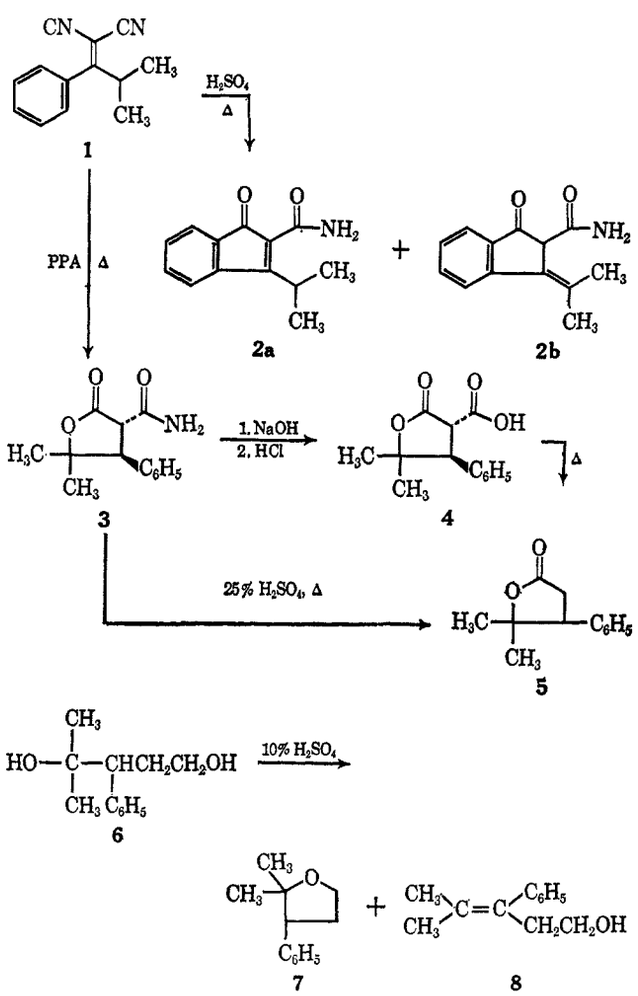
Initial treatment of ylidenemalononitriles in strong mineral acids such as concentrated sulfuric acid usually produced ketones, both aromatic and nonaromatic, but, when α-cyano-β-isopropylcinnamonitrile (**1**) was cyclized with polyphosphoric acid, α-carboxamido-β-phenyl-γ-methyl-γ-valerolactone (**3**) was produced. It was found in general that ylidenemalononitriles, bearing at least one γ hydrogen, upon treatment with polyphosphoric acid produced the γ-lactones in moderate to good yields. Substrates containing a tertiary γ hydrogen produced lactones in the highest yields and therefore this reaction may be used to produce γ-lactones by a new synthetic pathway. Compound **3** was characterized by hydrolysis, decarboxylation, reduction to 3-phenyl-4-methylpentane-1,4-diol (**6**), and cyclization to 2,2-dimethyl-3-phenyltetrahydrofuran (**7**).

During the course of continued investigation of ylidenemalononitriles in these laboratories,[1-4] cyclizations have usually been carried out in concentrated sulfuric acid in preference to polyphosphoric acid since the latter has proved to be less reliable in the formation of ketones, either aromatic or nonaromatic. For example, when α-cyano-β-isopropylcinnamonitrile (**1**) was cyclized in concentrated sulfuric acid, both the indenone (**2a**) and indanone (**2b**) were isolated, but when **1** was cyclized with polyphosphoric acid, a different product was isolated which was characterized as α-carboxamido-β-phenyl-γ-methyl-γ-valerolactone (**3**).[5] A thorough examination of the products from both reactions by thin layer chromatography[6] revealed that the mother liquors from the sulfuric acid reaction contained 5–10% of the same lactone (based on total solids obtained) while no ketones were obtained from the polyphosphoric acid reaction. This is a most interesting result in view of the fact that cold concentrated sulfuric acid usually leads to lactones while hot polyphosphoric acid usually leads to ketones, at least in the cyclization of olefinic acids.[7] This initial result prompted us to investigate further cyclizations of ylidenemalononitriles bearing at least one γ hydrogen. Results indicated that this reaction was one of general utility and a novel method of preparing γ-substituted γ-valerolactones usually in better yields than the previously reported procedures which involved levulinate esters and Grignard reagents.[8,9]

SCHEME I



Results and Discussion

When α-cyano-β-isopropylcinnamonitrile (**1**) was cyclized with polyphosphoric acid, a crystalline product was obtained which was characterized as *trans*-α-carboxamido-β-phenyl-γ-methyl-γ-valerolactone (**3**) by analysis, spectral properties, and the degradative scheme shown in Scheme I. Compound **3** was hydrolyzed with 10% sodium hydroxide at room temperature, affording the corresponding acid α-carboxy-β-phenyl-γ-methyl-γ-valerolactone (**4**). Evolution of carbon dioxide on melting indicated that **4** was a β-oxo acid and produced β-phenyl-γ-methyl-γ-valerolactone (**5**). It was subsequently found that hydrolysis of **3** in 25% refluxing sulfuric acid yielded **5** directly in improved yield. To substantiate these results further, **5** was reduced with lithium aluminum hydride in refluxing ether to produce 4-methyl-3-phenyl-1,4-pentanediol (**6**). When **6** was refluxed with 10% sulfuric acid, a mixture of two liquid products was obtained which could be separated easily by gas chromatography. The two products, 2,2-dimethyl-3-phenyltetrahydrofuran (**7**) and 4-methyl-3-phenyl-3-penten-1-ol (**8**), were obtained in a 3:1 ratio. If **6** was refluxed in benzene with a catalytic amount of *p*-

(1) E. Campaigne and G. F. Bulbenko, *J. Org. Chem.*, **26**, 4703 (1961).
(2) E. Campaigne, G. F. Bulbenko, W. E. Kreighbaum, and D. R. Maulding, *ibid.*, **27**, 4428 (1962).
(3) E. Campaigne, D. R. Maulding, and W. R. Roelofs, *ibid.*, **29**, 1543 (1965).
(4) E. Campaigne and W. L. Roelofs, *ibid.*, **30**, 396 (1965).
(5) E. Campaigne and R. L. Ellis, *Chem. Commun.*, 141 (1966).
(6) Analysis of lactone in sulfuric acid reaction was carried out by a comparison of a diluted pure sample of lactone with a sample of total reaction product solids, using a quantitative analysis by development of the chromatograms with iodine, until the color of the spots were of equal intensity.
(7) M. F. Ansell and M. H. Palmer, *Quart. Rev.* (London), **18**, 211 (1964).
(8) S. Dev and C. Rai, *J. Indian Chem. Soc.*, **34**, 178 (1957).
(9) S. Dev and C. Rai, *ibid.*, **34**, 266 (1957).

TABLE I

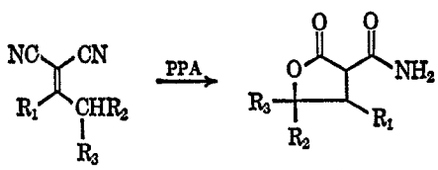
PROPERTIES OF YLIDENEMALONONITRILES

Compound	R	Bp or mp, °C (mm)	Yield, %	N, % Calcd	N, % Found
1		60–62	92[a]	*a*	
9a	$R_1 = C_6H_5$; $R_2, R_3 = -(CH_2)_5-$	77–78	96	11.86	11.86
9b	$R_1 = C_6H_5$; $R_2, R_3 = -(CH_2)_2-$	110–111	61[b]	14.42	14.40
9c	$R_1 = i\text{-}C_3H_7$; $R_2 = R_3 = CH_3$	60 (0.1)	54	17.30	17.42
9d	$R_1 = CH_3$; $R_2 = R_3 = CH_3$	47–49 (0.15)[c]	70	*c*	
9e	$R_1 = H$; $R_2 = R_3 = CH_3$	38–41 (0.4)	78	23.07	22.86
11a	$R_1 = H$	84–86 (0.8)[d]	92	*d*	
11b	$R_1 = CH_3$	72–75 (0.1)	96	17.49	17.19
13a	$R_1 = CH_3$	54–56 (0.5)	93	18.92	19.13
13b	$R_1 = C_6H_5$	67.5–69	59	13.32	13.24
15		154–155[e]	40	*e*	

[a] Reference 2. [b] Prepared from α-cyano-β-(3-chloropropyl)cinnamonitrile. [c] H. D. Edwards, F. P. Doyle, and S. J. Pauling, U. S. Patent 2,839,402 (1958); *Chem. Abstr.*, **53**, 943c (1958). [d] A. C. Cope and K. E. Hoyle, *J. Am. Chem. Soc.*, **63**, 733 (1941). [e] E. Campaigne, R. Subramanya, and D. R. Maulding, *J. Org. Chem.*, **28**, 623 (1963).

TABLE II

PROPERTIES OF LACTONES



9 10

Compound	R	Lactone	Yield, %	Mp, °C	N, % Calcd	N, % Found
1		3	86	172–173.5	6.01	5.80
9a	$R_1 = C_6H_5$; $R_2, R_3 = -(CH_2)_5-$	10a	83[a]	232–234	5.13	5.23
9b	$R_1 = C_6H_5$; $R_2, R_3 = -(CH_2)_2-$	10b	7[a]	179–181	6.06	6.07
9c	$R_1 = i\text{-}C_3H_7$; $R_2 = R_3 = CH_3$	10c	61	139–141	7.00	7.20
9d	$R_1 = CH_3$; $R_2 = R_3 = CH_3$	10d	48	119–120	8.18	8.31
9e	$R_1 = H$; $R_2 = R_3 = CH_3$	10e	27	134–136	8.92	9.06

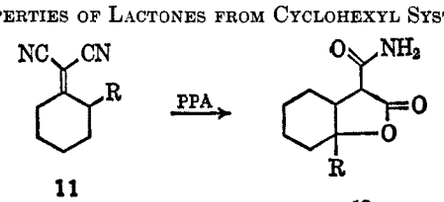
[a] Spirolactones.

toluenesulfonic acid, **7** was isolated in high yield and 97% pure by gas chromatography.

To determine the generality of this ring closure, a number of ylidenemalononitriles were examined (see Table I). The preparations of these compounds usually occur in very good yields, since unreacted starting ketones were recovered by distillation. The products from the cyclization are shown in Tables II and III.

TABLE III

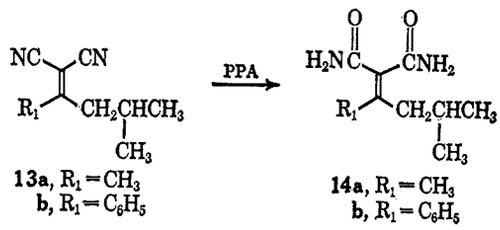
PROPERTIES OF LACTONES FROM CYCLOHEXYL SYSTEMS



11 12

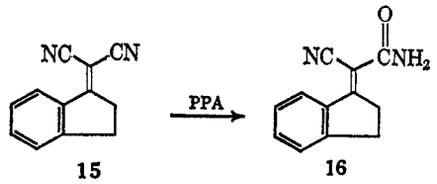
Compound	R	Lactone	Yield, %	Mp, °C	N, % Calcd	N, % Found
11a	$R_1 = H$	12a	46	172–174	7.65	7.75
11b	$R_1 = CH_3$	12b	80	115–117	7.10	7.00

Since we had shown that γ-lactones can be formed from aliphatic ylidenemalononitrile systems and that cyclization to a tertiary carbon occurred in higher yield than to a secondary carbon, it was desirable to examine an aliphatic ylidenemalononitrile which offered a choice of cyclization at a γ secondary carbon forming a γ-lactone or a δ tertiary carbon yielding a δ-lactone. δ-Lactones had not been obtained in this reaction. When the reaction was carried out employing 1,1-dicyano-2,4-dimethyl-1-pentene (**13a**), only the corresponding diamide **14a** was obtained. Similarly, when α-cyano-β-isobutylcinnamonitrile (**13b**) was treated with polyphosphoric acid, the corresponding diamide **14b** was obtained as the only product. These observations would indicate only tertiary carbon atoms at a γ position can enter into the cyclization reaction in open-chain systems and steric factors are important in the formation of lactones in these systems. These factors are apparently restricted in the cyclohexylidene



13a, $R_1 = CH_3$
b, $R_1 = C_6H_5$

14a, $R_1 = CH_3$
b, $R_1 = C_6H_5$



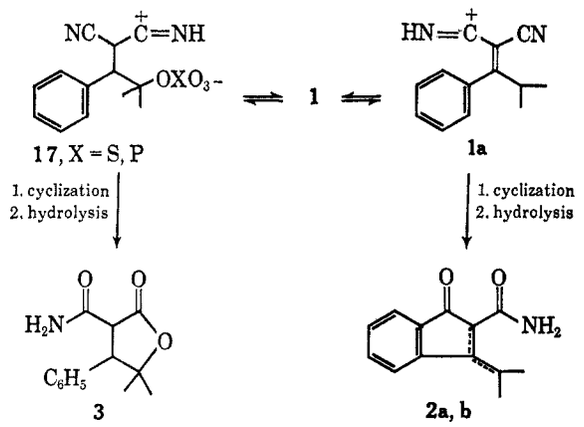
15 16

series. Also when 1-indanylidenemalononitrile (**15**) was treated with polyphosphoric acid, only the cor-

responding monoamide **16** was isolated, as was the case when this ylidenemalononitrile was treated with concentrated sulfuric acid.[8]

It is apparent that cyclization is favored at a γ tertiary carbon atom and that yields are always higher in these cases. For example, cyclic ylidenemalononitrile **11h** produces only the lactone with the bridgehead methyl group (**12b**) and no isolable lactone derived from cyclization at the other possible γ carbon atom. Furthermore, the yields vary in a direct relationship to the function R_1 (aryl > alkyl > H) in any series; the yields are not so variable with R_2 and R_3 as long as they are both alkyl (see Table II).

Conversion of unsaturated acids to lactones regardless of the relative positions of the double bond and the carboxyl group, provided that the double bond is able to migrate (even in some cases with skeletal rearrangement), is well documented.[7] The formation of lactones directly from unsaturated nitriles is far less common[10] and these have not involved migration of the double bond. While a plausible mechanism for the conversion of unsaturated acids, esters, and amides is easily visualized,[7,11] it cannot be applied directly to the unsaturated nitrile system, since the incorporation of an additional atom of oxygen must be accounted for. When Raffauf[10] treated 2,2-diethyl-4-pentenenitrile with sulfuric acid, he obtained an imino ether and subsequently the corresponding lactone by aqueous acid hydrolysis, but, when the saturated derivative, 2,2-diethylvaleronitrile, was subjected to the same reaction conditions, he isolated no imino ether. This he offered as indirect evidence suggesting that the extra atom of oxygen is the result of initial addition of sulfuric acid to the double bond followed by cyclization with the displacement of an oxidized sulfur to form the imino ether. The different results obtained when **1** is treated in sulfuric acid compared with treatment with polyphosphoric acid may be accounted for by a difference in ease of displacement of oxidized phosphorus in polyphosphate over ease of displacement of oxidized sulfur in sulfate. Thus **1** in sulfuric or polyphosphoric acid solution yields an equilibrium mixture of **17** (X = S or P) and protonated **1** (**1a**). Conversion of **17** (X = P) to **3** by displacement of oxidized phosphorus is more rapid than conversion of **1a** to **2a,b**, while the corresponding reaction of **17** (X = S) is much slower.



(10) R. F. Raffauf, *J. Am. Chem. Soc.*, **74**, 4460 (1952).
(11) P. N. Craig, *ibid.*, **74**, 129 (1952).

Experimental Section

All melting points reported were obtained from a Mel-Temp capillary melting point apparatus and were corrected. The microanalysis were performed by Midwest Microlab, Inc., Indianapolis, Ind. Infrared spectra were recorded with a Perkin-Elmer Model 137 or 137A Infracord. The ultraviolet spectra were recorded using a Bausch and Lomb Model 505 spectrophotometer. The nmr spectra were recorded on a Varian Model A-60 spectrometer, employing tetramethylsilane as an internal reference. All nmr spectra are in agreement with the assigned structures. The molecular weights were determined in specified solvents on a Mechrolab vapor pressure osmometer, Model 301A.

Preparation of Ylidenemalononitriles.—The method described by Mowry[12] was used for the preparation of all the ylidenemalononitriles except **9c**. Using the suggestion offered by Cope and co-workers,[13] an additional amount of catalyst was used for the condensation of malononitrile with hindered ketones. The general procedure for the condensation of nonhindered carbonyl compounds with malononitrile used in these experiments is described as follows. For every 0.5 mole of carbonyl compound, 0.6 mole of malononitrile, 4 g of anhydrous ammonium acetate, and 12 ml of glacial acetic acid were used. Anhydrous benzene was added and the benzene solution was refluxed until the amount of water collected in the Dean–Stark trap remained constant (usually 4–12 hr). For sterically hindered carbonyl compounds, the reflux time was longer and two to eight times the recommended amount of catalyst was added. After refluxing, the benzene solution was washed with water, bicarbonate solution, and water again, and dried (Na_2SO_4). Evaporation of the solvent yielded either a crystalline dinitrile or an oil. The latter compounds were distilled at reduced pressure (in some cases unreacted carbonyl compounds may be recovered). The properties of the ylidenemalononitriles prepared are summarized in Table I.

General Preparation of Lactones Using PPA.—The liquid ylidenemalononitriles were mixed thoroughly, using a mechanical stirrer, with ten times their weight of polyphosphoric acid at room temperature. When mixing was complete, the mixture was heated to 100° for 12 hr with continuous stirring. The mixtures were hydrolyzed in a tenfold weight of water. The solid ylidenemalononitriles were treated in a similar manner except that no mixing was required before heating. The mixtures were hydrolyzed as mentioned above. The hydrolyzed mixtures were saturated with NaCl and extracted with $CHCl_3$ if water-soluble products were obtained. The $CHCl_3$ solutions were washed with small volumes of water and dried (Na_2SO_4). The dry solutions were concentrated at reduced pressure to dryness and the resulting products were crystallized from ethyl acetate with subsequent addition of cyclohexane (2:1 to 1:1 ratio). The solid products which precipitated from the aqueous solutions were cooled, filtered, washed well with water, dried in a desiccator under reduced pressure, and recrystallized from ethyl acetate (small volumes of cyclohexane may be added to induce crystals). The following is a specific example.

α-Carboxamido-β-phenyl-γ-methyl-γ-valerolactone (3).—To 50 g of polyphosphoric acid in a beaker equipped with a mechanical stirrer was added 5 g (255 mmoles) of **1**. The mixture was then heated to 100° for 12 hr with stirring. The viscous mixture was hydrolyzed in 500 ml of water while still warm. After the hydrolyzed mixture had cooled to room temperature, the product which crystallized was filtered, washed well with water, dried at reduced pressure, and recrystallized from ethyl acetate and a small amount of cyclohexane, yielding 5 g (85%) or white crystals: mp 172–173.5; ν_{max}^{KBr} 3510 (NH), 3390 (NH), 1750 (CO), and 1700 (amide CO). The nmr spectrum (CF_3COOH) showed a singlet at δ 7.39 (5 H), a quartet at δ 4.33 (2 H) (J = 13 cps), a singlet at δ 1.64 (3 H), and a singlet at δ 1.17 (3 H). There was no ultraviolet absorption above 210 mμ. *Anal.* Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01; mol wt, 233. Found: C, 67.17; H, 6.43; N, 5.80; mol wt ($CHCl_3$), 240. The yields and properties of other lactones synthesized are reported in Tables II and III.

α-Carboxy-β-phenyl-γ-methyl-γ-valerolactone (4).—A solution of 1 g (4.3 mmoles) of **3** in 15 ml of 10% sodium hydroxide was stirred at room temperature until no further evolution of ammonia was detected by litmus tests (about 8 hr), then cooled to 0° in an ice bath, and acidified with concentrated hydrochloric acid.

(12) D. T. Mowry, *J. Am. Chem. Soc.*, **67**, 1050 (1945).
(13) A. C. Cope, C. M. Hofmann, C. Wyckoff, and E. Hardenberg, *ibid.*, **63**, 3452 (1944).

The resulting white solid was filtered, washed well with water, and dried at reduced pressure. The dry solid was recrystallized from ethyl acetate yielding 0.85 g (85%) of white crystals: mp 156–157° dec; ν_{max}^{KBr} 2565 (CO_2H), 1755 (CO), and 1720 (acid CO). The nmr spectrum (CF_3COOH) had δ 7.37 (singlet, 5 H), 4.36 (quartet, 2 H) (J = 13 cps), 1.65 (singlet, 3 H), 1.17 (singlet, 3 H). *Anal.* Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02; mol wt, 234. Found: C, 66.93; H, 5.98; mol wt (bromthymol blue in ethanol), 235.

β-Phenyl-γ-methyl-γ-valerolactone (5). A.—In an open reaction vessel, 2 g (8.5 mmoles) of **4** was heated in a oil bath to 180–190° until evolution of carbon dioxide ceased (about 10 min). Upon cooling of the residue to room temperature, the product solidified and was crystallized from benzene and hexane (1:1) yielding 1.3 g (80%) of white crystals: mp 91–92°; ν_{max}^{KBr} 1765 (CO). *Anal.* Calcd for $C_{12}H_{14}O_2$: C, 75.75; H, 7.43; mol wt, 190. Found: C, 75.88; H, 7.63; mol wt ($CHCl_3$), 189.

B.—To 50 ml of 20% sulfuric acid was added 4.66 g (20 mmoles) of **1**. The resulting mixture was heated at reflux with stirring for 16 hr. After cooling, the resulting oil solidified. The solid was filtered, washed well with water, and dried at reduced pressure. The product was dissolved in about 50 ml of benzene, decolorized with Norit A, filtered, and concentrated to one-half its initial volume. When 10–15 ml of cyclohexane was added, the product (3.45 g, 91%) crystallized as white plates, mp 90.5–92.

4-Methyl-3-phenyl-1,4-pentanediol (6).—Anhydrous ether (500 ml) followed by $LiAlH_4$ (2.25 g, 60 mmole) was introduced into a round-bottom flask equipped with a magnetic stirrer and heating mantle. In a modified liquid–liquid continuous extractor there was added 15 g (80 mmoles) of **5**. The column was filled with ether and the pot containing the hydride solution was heated at reflux for 12 hr (necessary procedure since the solid lactone is only slightly soluble in ether). After cooling of the reaction mixture, the hydride solution was cautiously hydrolyzed with saturated Na_2SO_4 solution. The resulting salts were dissolved in 10% hydrochloric acid and the layers separated. The aqueous solution was extracted with an additional 100 ml of ether. The combined ether solutions were washed with water, $NaHCO_3$ solution, and water again, then dried (Na_2SO_4), and concentrated to dryness at reduced pressure, giving a white solid which was recrystallized from benzene yielding 14 g (91%) or white needles: mp 89–90°; ν_{max}^{KBr} 3290 (H-bonded OH, broad), 1065 (primary COH stretch), and 1135 (tertiary COH stretch). *Anal.* Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.31; H, 9.31.

2,2-Dimethyl-3-phenyltetrahydrofuran (7) and 4-Methyl-3-phenyl-3-penten-1-ol (8).—A solution of 40 ml of 10% sulfuric acid containing 3.88 g (20 mmoles) of diol **6** was stirred at reflux for 90 min, cooled to room temperature, and neutralized with Na_2CO_3. The neutralized solution was extracted twice with 50-ml portions of ether. The extracts were washed with water twice, dried (Na_2SO_4), and concentrated at reduced pressure to yield 3 g (85%) of an oil. Analysis by gas chromatography on an 8-ft 20% Carbowax on Diataport S support at 238° (helium flow, 60 cc/min) gave two components in a 3:1 ratio with retention times of 4.5 min (**7**) and 8.5 min (**8**), respectively. Infrared absorption of **7** showed no hydroxyl absorption but exhibited absorption at 1135 (ether) and was nonviscous with $n^{27}D$ 1.5160. The nmr in $CDCl_3$ showed a singlet at δ 7.07 (5 H), a multiplet at δ 3.85 (2 H), a triplet at δ 2.96 (J = 8.5 cps) (1 H), a multiplet at δ 2.21 (2 H), a singlet at δ 1.27 (3 H), and a singlet at δ 0.81 (3 H). Compound **8**, ν_{max}^{neat} 3290 (OH, broad), 1595 (C=C), was viscous with $n^{27}D$ 1.5360. The nmr of **8** ($CDCl_3$) exhibited a multiplet at δ 7.01 (5 H), a triplet at δ 3.40 (J = 7 cps) (2 H), a triplet at δ 2.54 (J = 7 cps) (2 H), a singlet at δ 1.78 (3 H), and a singlet at δ 1.50 (3 H). The hydroxyl proton absorption occurred at δ 2.45, but it is well known that the hydroxyl frequencies of alcohols can vary over a wide range according to the nature of the solvent, concentration of the solute, and temperature.[14] *Anal.* Calcd for **7**, $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.87; H, 9.44. *Anal.* Calcd for **8**, $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.51; H, 9.33. Similar ratios of products were obtained when **6** was refluxed in 10% H_2SO_4 for 15 min or in 1% H_2SO_4 for 2 hr.

2,2-Dimethyl-3-phenyltetrahydrofuran (7).—Diol **6** (1 g, 5.15 mmoles) was added to a solution of 10 ml of anhydrous benzene containing 100 mg of *p*-toluenesulfonic acid (prepared from the hydrate by azeotroping with benzene). This mixture was stirred at reflux for 1 hr. After cooling, the solution was washed with $NaHCO_3$ solution and water and dried (Na_2SO_4). Then this was concentrated at reduced pressure to yield 0.8 g (88%) of **7**. Gas chromatographic analysis as presented above showed an identical retention time with 97% purity of compound **7**.

α-Cyano-β-cyclopropylcinnamonitrile (9b).[15]—The starting material, α-cyano-β-(3-chloropropyl)cinnamonitrile, was prepared in the usual manner as described above. To 50 ml of benzene was added 6.2 g (27 mmoles) of α-cyano-β-(3-chloropropyl)cinnamonitrile and 2.3 g (27 mmoles) of piperidine. The solution was stirred at reflux for 6 hr, then the resulting dark orange slurry was cooled to about 5° and filtered (3.1 g (93%) of piperidine hydrochloride was obtained). The filtrate was washed with saturated $NaHCO_3$ solution and water and dried (Na_2SO_4). The dried solution was concentrated at reduced pressure to dryness and the resulting solid was taken up into ethanol, treated with Norit A, filtered while hot, and allowed to crystallize, yielding 3.2 g (61%) of white crystals: mp 110–111°; ν_{max}^{KBr} 3050 (cyclopropyl CH), 1020 (skeletal C_3H_5), and 2250 (CN). *Anal.* Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19; N, 14.42. Found: C, 80.44; H, 5.50; N, 14.40.

α-Carboxamido-β-phenyl-γ-spirocyclopropylbutyrolactone (10b).—Compound **9b** (10 g, 51 mmoles) was added to 100 g of polyphosphoric acid with stirring. The resulting mixture was heated to 100° for 8 hr during which time the reaction mixture turned dark orange. The mixture was hydrolyzed in 1 l. of water and the aqueous solution saturated with NaCl and extracted with three 100-ml portions of $CHCl_3$. The combined extract was washed with a small volume of water, dried (Na_2SO_4), and concentrated at reduced pressure to yield an orange foam. The foam (4 g) was chromatographed over 120 g of acid-washed alumina and eluted successively with 500 ml of benzene, 300 ml of 10% ether in benzene, 200 ml of 20% ether in benzene, 500 ml of 50% ether in benzene, and 200 ml of 75% ether in benzene. The 50 and 75% ether fractions yielded the product as a fluffy white solid. The solids were combined and recrystallized from ethyl acetate to yield 0.85 g (7%) of colorless needles: mp 179.5–181°; ν_{max}^{KBr} 3050 (CH stretch C_3H_5), 1720 (CO), 1650 (amide Co), and 3450 (amide NH); δ (CF_3COOH), singlet at 7.40 (5 H), triplet at 4.63 (2 H) (J = 6.0 cps), triplet at 2.91 (2 H) (J = 7.0 cps), triplet at 2.33 (2 H) (J = 7.0 cps).[16] *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.50; H, 5.67; N, 6.06. Found: C, 67.38; H, 5.79; N, 6.07.

Registry No.—**3**, 13192-31-9; **4**, 13133-95-4; **5**, 13133-96-5; **6**, 13133-97-6; **7**, 13133-98-7; **8**, 13133-99-8; **9a**; 13134-00-4; **9b**, 13134-01-5; **9c**, 13017-57-7; **9e**, 13134-03-7; **10a**, 6900-16-9; **10b**, 13169-33-0; **10c**, 7128-62-3; **10d**, 13134-06-0; **10e**, 6989-68-0; **11b**, 13017-64-6; **12a**, 13134-09-3; **12b**, 13134-10-6; **13a**, 13134-11-7; **13b**, 13134-12-8.

Acknowledgment.—We gratefully acknowledge the support of this research by Public Health Service Fellowship No. 1-F1-GM-38,723 and by Grant GM-10366 to Indiana University.

(14) L. M. Jackman, "Organic Chemistry," Pergamon Press Ltd., London, England, 1963, p 69.

(15) We are indebted to Dr. W. E. Kreighbaum of these laboratories for the synthesis of this compound and an analytical sample. The procedure here is slightly modified, resulting in an improved yield.

(16) The lower J value for the C_2 and C_3 protons (7.0 cps) in this spirocyclopropyllactone **10b** compared with that of the dimethyllactone **3** (J = 13 cps) indicates a greater distortion of the C_3 atom out of the plane of the lactone ring (*cf.* G. A. Jeffrey and S. H. Kim, *Chem. Commun.*, No. 7, 211 (1966).