An attempt to prepare the O,N-diacetyl derivative by refluxing the amino amide VII (R = cyclohexyl) with excess acetyl chloride for 48 hr. failed. Only the mono-O-acetyl derivative could be obtained *even in the presence of excess triethylamine.*

Substituting propionyl chloride for the acetyl chloride in the foregoing procedure gave the similarly ether soluble **N-cyclohexyl-β-cyclohexylamino-α-(o-propionoxyphenyl)-α-phenylpropionamide hydrochloride (XIc)** in 53% yield, m.p. 190–191°, $\lambda_{max}^{CHCl_3}$ 5.69 μ (ester >C=O), 5.98 μ (amide >C=O).

Anal. Calcd. for $C_{30}H_{41}ClN_2O_3$: C, 70.22; H, 8.06; N, 5.46. Found: C, 70.18; H, 8.06; N, 5.67.

Substituting the amino amide VII (R = cyclopropyl) for the cyclohexyl analog and ethyl chloroformate for the acetyl chloride in the foregoing procedure gave **N-cyclopropyl-β-cyclopropylamino-α-(o-ethoxycarbonyloxy)-α-phenylpropionamide hydrochloride (XIa)**, m.p. 177–178°, $\lambda_{max}^{CHCl_3}$ 1.49 μ (NH), 1.63 μ (cyclopropyl), 5.69 μ (ester >C=O), 5.89 μ (amide >C=O).

Anal. Calcd. for $C_{24}H_{29}ClN_2O_4$: C, 64.77; H, 6.57; N, 6.30; O, 14.38. Found: C, 64.62; H, 6.39; N, 6.29; O, 14.57.

Treatment of the amino acetamide V (R = cyclohexyl) with acetyl chloride according to the above procedure and isolation of the product as the base gave, in 45% yield, **N-cyclohexyl-α-cyclohexylamino-α-(o-acetoxyphenyl)-α-phenylacetamide (Xa)**, m.p. 143–144°, $\lambda_{max}^{CHCl_3}$ (μ) 3.02 (NH), 5.67 (ester >C=O), 6.01 (amide >C=O).

Anal. Calcd. for $C_{28}H_{36}N_2O_3$: C, 74.97; H, 8.09; N, 6.24. Found: C, 75.07; H, 8.14; N, 6.31.

Likewise, from propionyl chloride and V (R = cyclohexyl) was obtained in 40% yield, **N-cyclohexyl-α-cyclohexylamino-α-(o-propionoxyphenyl)-α-phenylacetamide (Xb)**, m.p. 118–119°, $\lambda_{max}^{CHCl_3}$ (μ) 3.01 (NH), 5.68 (ester >C=O), 6.01 (amide >C=O).

Anal. Calcd. for $C_{29}H_{38}N_2O_3$: C, 75.29; H, 8.28; N, 6.05. Found: C, 75.74; H, 8.39; N, 5.77.

Acknowledgment—We wish to thank Mr. Dave Wimer for the potentiometric titrations; Mr. W. H. Washburn for the infrared spectra; Mr. E. F. Shelberg and associates for the microanalyses; Mr. G. M. Bradford and Mr. N. F. Ryan for technical assistance; and Mr. T. F. Page, Jr., Battelle Memorial Institute, and Dr. R. W. Mattoon for the n.m.r. spectra.

Neighboring Group Reactions. IX. Some Cyclic Imidates and Related Lactones with Functional Substituents

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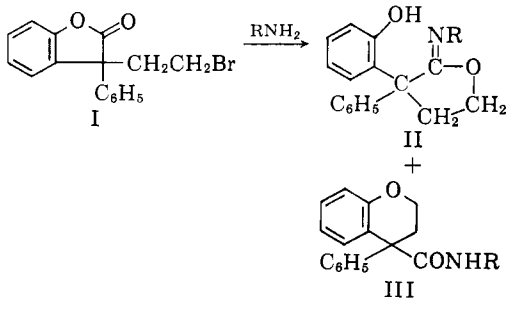
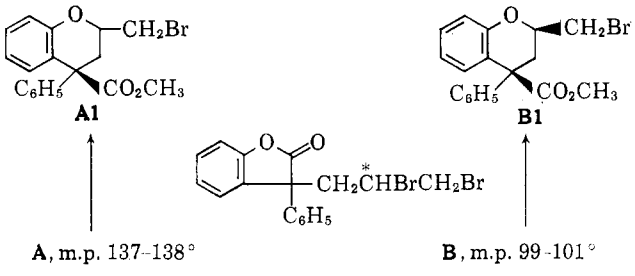
Cyclopropylamine effects preferential and stereospecific intramolecular displacement of the 2′-bromine atom from the two diastereoisomers **A** and **B** of 3-(2′,3′-dibromopropyl)-3-phenyl-2-benzofuranone. Fair yields (60–70%) of the geometrically isomeric cyclic imidates **A2** and **B2** result. The multiplicity and variable proximity of functional groups in these compounds, as well as in the isomeric lactones (**A4** and **B4**) derived from them, lead to a variety of intramolecular reactions. These are summarized in the accompanying flow chart.

The purpose of the present work was the development of a synthetic sequence derived from the combination of results reported in two previous papers of this series. The accompaning paper[1] described the reaction of 3-(β-bromoethyl)-3-phenyl-2-benzofuranone (I) with primary amines. Products consisted of varying amounts of cyclic imidates II and rearranged amides III. Another report[2] described the reactions of the two diastereoisomeric dibromopropylbenzofuranones **A** and **B** with sodium methoxide. In each case preferential and stereospecific displacement of the secondary bromine atom occurred with rearrangement to give the geometrically isomeric bromo esters **A1** and **B1**,[3] respectively, in good yields (89–96%). Similar selective behavior of **A** and **B** toward primary amines, analogous to that of I to produce II, would be expected to yield products possessing an unusual combination of functional groups in a single molecule. Cyclopropylamine was chosen to verify this expectation because it, of all the primary amines used[1] in reactions with I, produced the best yields of II at the expense of III. Reactions of **A** and **B** with cyclopropylamine and subsequent transformations of the resulting products are outlined in the attendant chart.





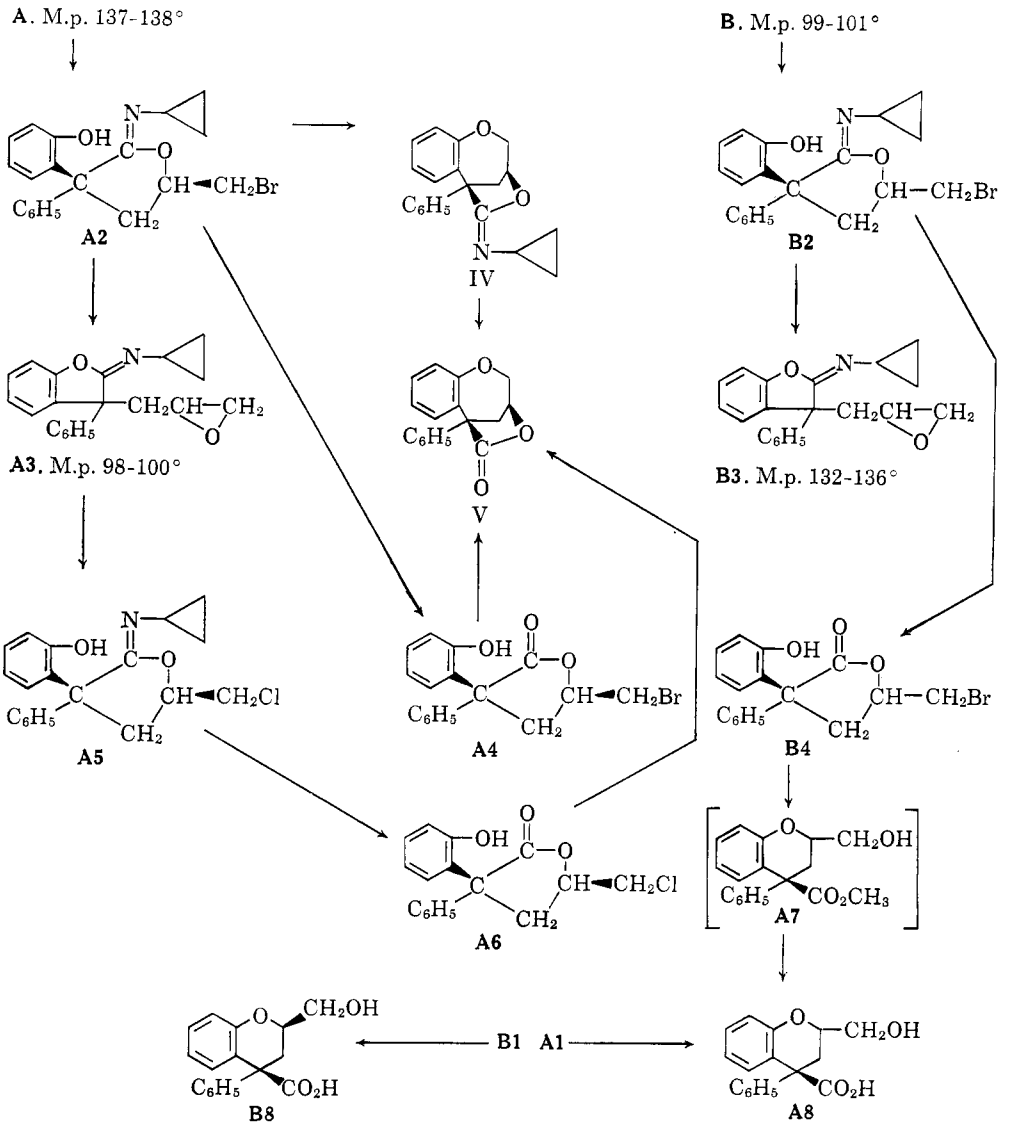
Treatment of the isomeric dibromides **A** and **B** with cyclopropylamine at room temperature gave the expected cyclic imidates **A2** and **B2**, respectively, in 73% and 58% yields.[4] These products each contain two electrophilic carbon atoms (>C=N— and —CH_2Br)

(1) H. E. Zaugg, R. W. DeNet, and R. J. Michaels, *J. Org. Chem.*, **28**, 1795 (1963).

(2) H. E. Zaugg, R. W. DeNet, and E. T. Kimura, *J. Med. Pharm. Chem.*, **5**, 430 (1962).

(3) The notational convention used in this paper is designed to facilitate recognition of the steric relationships among isomers. For example, all products derived from **A**, m.p. 137–138°, by only one inversion at the carbon atom marked with an asterisk, are members of the **A** family. The **B** family derives similarly from **B**, m.p. 99–101°. It follows that two inversions at this asymmetric center effect family interconversion. Two compounds with the same number (*e.g.*, **A1**, **B1**) constitute diastereoisomeric pairs.

(4) The infrared spectra of these bases were typical of this structure (*i.e.*, II[1]), namely broad and weak absorption centered at 3.9 μ (bonded OH) and strong absorption at 5.87–5.88 μ (C=N). The neutral fractions of these reactions were not examined for the presence of rearranged amide [*i.e.*, the 2-bromomethyl derivative of III (R = cyclopropyl)].



and a potentially available nucleophilic center ($ArOH \rightarrow ArO^{\ominus}$). However, only in the *cis*-bromophenol **A2**[5] does the phenoxide ion (generated by treatment with base) have the option of reacting with either or both of these electrophilic centers. Thus, treatment of **A2** with an equivalent of sodium methoxide in 1,2-dimethoxyethane gave an 86% yield of the bridged bicyclic imidate IV,[6] the product of direct bromide ion displacement by the phenoxide oxygen atom. In methanol solution, however, the yield of IV was reduced to 46% and a 33% yield of the epoxyimidate **A3** was secured.[7] From the *trans*-bromophenol **B2**, on the other hand, the isomeric epoxyimidate **B3** was the only isolable product (58% yield).[8]

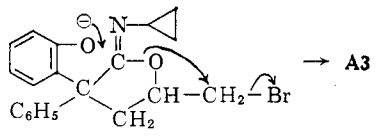
The structure assigned to **A3** (and **B3**) was supported by its reaction with ethereal hydrogen chloride. It gave in 69% yield the hydrochloride of **A5** which is the chloro analog of **A2**.[10] Acid hydrolysis of **A5** gave the phenolic γ-lactone **A6** (91% yield) which with sodium methoxide cyclized (65% yield) to the bridged γ-lactone V,[6] identical with the lactone obtained (97% yield) from acid hydrolysis of the bridged bicyclic imidate IV.

Acid hydrolysis of the two cyclic imidates **A2** and **B2** gave the corresponding lactones **A4** and **B4**, respectively, in 49% and 85% yields. These two isomers

(5) Since the geometry of **A1** was known,[2] the reasonable assumption that formation of **A1** and **A2** both occur with complete inversion allowed the prediction that the cyclic imidate obtained from A would indeed have the structure (*i.e.*, **A2**) in which the bromomethyl and phenolic groups would both be on the same side of the plane defined by the heterocycle.

(6) The assignment of structure is documented in Experimental.

(7) Formation of **A3** can be envisaged as a concerted intramolecular process induced by initial attack of phenoxide ion at the imino carbon atom of **A2**.



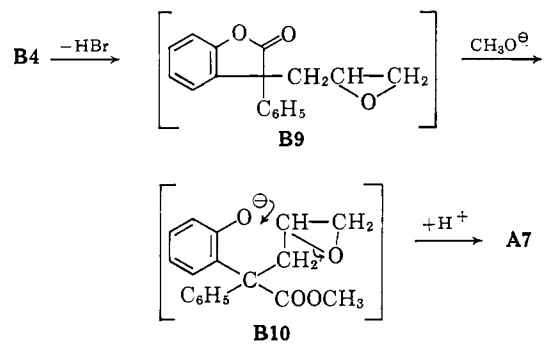
(8) The presence of the epoxide ring in **A3** and **B3** could not be demonstrated unequivocally by the near infrared correlation at 1.63 μ because of the cyclopropyl ring in the same molecule (the 1.63-μ band is characteristic of a $-CH_2-$ group in a three-membered ring).[9] However, the intensity of this absorption in both **A3** and **B3** was distinctly greater than that in IV, suggesting the presence in them of more than one three-membered ring.

The observed >C=N— absorption at 5.80 μ in both **A3** and **B3** is consistent with its occurrence at 5.87–5.88 μ in **A2** and **B2**. By analogy, lactone carbonyl absorption in benzofuranones (*e.g.*, I) occurs at 5.55 μ compared to 5.65 μ characteristic of saturated five-membered lactones.

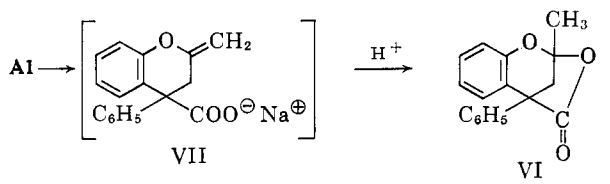
(9) W. H. Washburn and M. J. Mahoney, *J. Am. Chem. Soc.*, **80**, 504 (1958).

(10) The infrared spectra of **A2** and **A5** were nearly superimposable. This reaction with hydrogen chloride can be regarded as a concerted intramolecular process just the reverse of the one pictured[7] (**A3** from **A2**).

and the chloro analog **A6** all showed hydroxyl and carbonyl absorption in the infrared singularly characteristic[11] of this hydroxy lactone system. The *cis* isomer **A4**, like **A6**, led, as expected, to the bridged lactone V (65% yield). However, the *trans* isomer **B4**, with sodium methoxide, produced a hydroxy ester, **A7**, which could not be isolated in pure form but was saponified to the corresponding hydroxy acid **A8**, identical with a sample prepared from the bromo ester **A1** and different from the isomeric hydroxy acid **B8** derived from **B1**. Since it is highly unlikely that any, let alone total, inversion occurred in both processes **A1** → **A8** and **B1** → **B8**, this means that in going from **B4** to **A7** an inversion has occurred.[3] A reasonable mechanism to account for this involves the intermediacy of an epoxy lactone **B9** formed in the same way[7] as the epoxy imidates **A3** and **B3**. Attack of methoxide ion at the carbonyl group of **B9** followed by intramolecular reaction of the expelled phenoxide ion at the asymmetric epoxide carbon atom (accompanied by inversion, *i.e.*, **B10**) would produce the hydroxy ester, **A7**, of observed configuration.



Worthy of incidental note is the formation of the bridged lactone VI[6] as a by-product (31% yield) in the saponification of the bromo ester **A1**. Very likely it is produced as a result of combined dehydrobromination and hydrolysis to the salt of the unsaturated acid VII which, after acidification, cyclizes spontaneously to VI. Although the lactone VI could be formed from **B1** as well as from **A1**, none of it was isolated from this source. This suggests that bromide replacement in **B1** is anchimerically assisted by its ability to form the bridged δ-lactone[2] once the carboxylate ion is generated from the ester. Thus it competes more effectively than **A1** with the elimination reactions.



Experimental

***cis*-5-Bromomethyl-N-cyclopropyl-3-(*o*-hydroxyphenyl)-3-phenyl-2-tetrahydrofuranoneimine (A2).**—To a solution of 410 g. (1.0 mole) of 3-(2′,3′-dibromopropyl)-3-phenyl-2-benzofuranone (**A**), m.p. 137–138°,[2] in 2 l. of dry benzene was added, in a steady stream with stirring at 30°, 125 g. (2.2 moles) of cyclopropylamine. No heat of reaction was detectable. After stirring for 2 hr., the mixture was allowed to stand at room temperature for 1 week.

The precipitated cyclopropylamine hydrobromide (116 g., 84%, m.p. 149–153°) was removed by filtration and washed with benzene. The combined filtrate and washings were concentrated to dryness under reduced pressure. The oily residue was taken up in 500 ml. of chloroform and treated with 20% aqueous hydrochloric acid until no more salt precipitated. This salt was collected at the filter and washed with more chloroform. The combined filtrate and washings were separated from the aqueous layer and concentrated to dryness on the steam bath in order to recover unchanged dibromide **A** (49 g., 12%, m.p. 135–137°).

The crude hydrochloride was suspended in chloroform and treated with excess 20% aqueous sodium hydroxide. Separation and concentration of the chloroform solution to dryness gave a viscous oil which solidified. Two recrystallizations from 350–400 ml. of absolute ethanol gave **A2** (249 g., 64% conversion, 73% yield) of sufficient purity (m.p. 110–115°) for further use. A sample was recrystallized several more times to a constant m.p. 116–117°; $\lambda_{max}^{CHCl_3}$ (μ) 3.9 (broad and weak), 5.87 (s).

Anal. Calcd. for $C_{20}H_{20}BrNO_2$: C, 62.17; H, 5.22; N, 3.63. Found: C, 62.11; H, 5.47; N, 3.52.

A2 hydrochloride has m.p. 201–203° (from ethanol); λ_{max}^{Nujol} (μ) 5.97 (s).

Anal. Calcd. for $C_{20}H_{21}BrClNO_2$: C, 56.81; H, 5.00; N, 3.31. Found: C, 56.50; H, 5.00; N, 3.27.

A2 hydrobromide has m.p. 223–224° (from ethanol).

Anal. Calcd. for $C_{20}H_{21}Br_2NO_2$: C, 51.41; H, 4.53; N, 3.00. Found: C, 51.98; H, 4.66; N, 3.03.

***trans*-5-Bromomethyl-N-cyclopropyl-3-(*o*-hydroxyphenyl)-3-phenyl-2-tetrahydrofuranoneimine (B2).**—Application of the foregoing procedure to the diasterioisomeric dibromopropylbenzofuranone (**B**), m.p. 99–101°, gave a 58% yield of the *trans*-imidate **B2**, m.p. 146–147° (from ethanol); $\lambda_{max}^{CHCl_3}$ (μ) 3.9 (broad and weak), 5.88 (s).

Anal. Calcd. for $C_{20}H_{20}BrNO_2$: C, 62.17; H, 5.22; N, 3.63. Found: C, 62.29; H, 5.23; N, 3.43.

N-Cyclopropyl-3-(2′,3′-epoxypropyl)-3-phenyl-2-benzofuranoneimine (M.p. 132–136°) (B3).—A solution of 3.5 g. (0.009 mole) of the cyclic imidate **B2** in 50 ml. of dry 1,2-dimethoxyethane was refluxed and stirred for 16 hr. with 0.5 g. (0.009 mole) of sodium methoxide. The mixture was then concentrated to dryness under reduced pressure, treated with 50 ml. of water, and extracted with chloroform. From the chloroform layer, after separation and concentration to dryness, was obtained a semisolid product (2.7 g.) which was recrystallized three times from 95% ethanol to give the epoxide **B3** (1.6 g., 58%), m.p. 132–136°; $\lambda_{max}^{CS_2}$ 1.63 μ, no NH or OH absorption; $\lambda_{max}^{CHCl_3}$ (μ) 5.80 (s). The infrared spectrum in the 3–8-μ region was qualitatively identical to that of the isomer **A3**.

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.65; H, 6.28; N, 4.59. Found: C, 78.40; H, 5.97; N, 4.39.

4,5-Benzo-7-cyclopropylimino-3,8-dioxa-6-phenylbicyclo[4.2.1]nonane (IV).—Extension of the foregoing procedure to the isomeric cyclic imidate **A2**, m.p. 116–117° (105.2 g., 0.272 mole), using 15.1 g. (0.28 mole) of sodium methoxide in 325 ml. of 1,2-dimethoxyethane gave 71.9 g. (86%) of IV, m.p. 186–188°. Recrystallization of a sample from dry ethanol to constant melting point gave pure IV, m.p. 190–191°; $\lambda_{max}^{CHCl_3}$ (μ) 1.63 (cyclopropyl-CH_2), 5.90 (s), no NH or OH absorption; 60-Mc. chemical shifts (c.p.s.) from tetramethylsilane in deuteriochloroform solution with relative areas in parentheses, assuming 9 aromatic protons: 25–50 (4), 123–181 (2), 181–225 (1), 225–283 (2), 283–302 (1), 388–480 (9, assumed) (total area corresponds to 19 protons).

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.65; H, 6.28; N, 4.59; O, 10.48. Found: C, 78.61; H, 6.06; N, 4.51; O, 10.58.

N-Cyclopropyl-3-(2′,3′-epoxypropyl)-3-phenyl-2-benzofuranoneimine (M.p. 98–100°) (A3).—A solution of 20.8 g. (0.054 mole) of cyclic imidate **A2** in 75 ml. of dry methanol was stirred for 4 days at room temperature with an equivalent quantity of sodium methoxide. Filtration of the reaction mixture gave directly, 7.6 g. (46%) of the bridged imidate IV, m.p. 189–190°. The filtrate was concentrated to dryness under reduced pressure and the residue was taken up in a mixture of ether (150 ml.) and water. The ether layer was separated, washed with two portions (30 ml.) of cold 10% hydrochloric acid, dried (anhydrous magnesium sulfate, and concentrated to dryness. The residual oil (5.5 g., 33%) solidified, m.p. 95–100°, and a sample was recrostallized twice from 95% ethanol to give the epoxide **A3**, m.p. 98–100°; $\lambda_{max}^{CS_2}$ 1.63 μ, no NH or OH absorption; $\lambda_{max}^{CHCl_3}$ (μ) 5.80 (s).

(11) H. E. Zaugg, R. W. DeNet, R. J. Michaels, W. H. Washburn, and F. E. Chadde, *J. Org. Chem.*, **26**, 4753 (1961).

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.65; H, 6.28; N, 4.59. Found: C, 78.47; H, 6.28; N, 4.38.

trans-**5-Bromo-4-hydroxy-2-(*o*-hydroxyphenyl)-2-phenylvaleric Acid γ-Lactone (B4)**—A mixture of 5.9 g. (0.015 mole) of the *trans*-cyclic imidate **B2**, 40 ml. of 12% aqueous hydrobromic acid, and 10 ml. of glacial acetic acid was heated on the steam bath for 5 hr. The mixture was concentrated to dryness under reduced pressure, the residue was taken up in benzene, washed with three portions of water, and concentrated once more to dryness. The residue (4.5 g., 85%, m.p. 110–115°) was recrystallized three times from a benzene–hexane mixture to give 2.1 g. of the γ-lactone **B4**, m.p. 120° to a turbid melt clearing at 133°; $\lambda_{max}^{CHCl_3}$ (μ) 2.8 (w), 3.0 (w), 5.65 (m) (sh), 5.74 (s), 6.21 (w), 6.33 (w), 6.74 (m). (This combination of bands is nearly identical to that found[11] for the corresponding lactone, lacking only the bromomethyl group of **B4**.)

Anal. Calcd. for $C_{17}H_{15}BrO_3$: C, 58.81; H, 4.36; O, 13.82. Found: C, 58.97; H, 4.46; O, 13.94.

cis-**5-Bromo-4-hydroxy-2-(*o*-hydroxyphenyl)-2-phenylvaleric Acid γ-Lactone (A4)**.—Treatment of 8.5 g. (0.22 mole) of the *cis*-cyclic imidate **A2** according to the foregoing procedure, gave 2.7 g. (26%) of unchanged **A2** isolated as the hydrobromide, m.p. 222–223°, and 3.7 g. (49%) of **A4**, m.p. 201–203° (from ethanol; insoluble in chloroform); λ_{max}^{Nujol} (μ) 2.98 (m), 5.72 (s). (The weak absorption at 2.8 μ and the shoulder at 5.65 μ which appear in chloroform solution are absent in the solid spectra of these lactones. This is consistent with the view that, in the solid phase, these substances exist entirely in the >C=O· · · HO— bonded form).[11]

Anal. Calcd. for $C_{17}H_{15}BrO_3$: C, 58.81; H, 4.36; O, 13.82. Found: C, 59.09; H, 4.53; O, 14.21.

cis-**5-Chloromethyl-N-cyclopropyl-3-(*o*-hydroxyphenyl)-3-phenyl-2-tetrahydrofuranoneimine (A5)**.—A solution of 2.7 g. (0.0088 mole) of the epoxide **A3**, m.p. 98–100°, in dry ether was treated with excess ethereal hydrogen chloride. The precipitated salt was collected at the filter and recrystallized twice from a dry ethanol–ether mixture to give 2.3 g. (69%) of **A5** hydrochloride, m.p. 199–200°; λ_{max}^{Nujol} (μ) 6.00 (s).

Anal. Calcd. for $C_{20}H_{21}Cl_2NO_2$: C, 63.49; H, 5.60; N, 3.71; Cl (total), 18.74; Cl (ionic), 9.37. Found: C, 63.51; H, 5.54; N, 3.78; Cl (total), 18.64; Cl (ionic), 9.16.

Treatment of an aqueous solution of the hydrochloride (0.8 g.) with sodium bicarbonate precipitated the corresponding base which was recrystallized from 95% ethanol to give pure **A5** (0.5 g., 70%), m.p. 105–106°; $\lambda_{max}^{CHCl_3}$ (μ) 3.9 (broad and weak), 5.87 (s). Except for slight differences in the 9–10-μ region its infrared spectrum (chloroform) was qualitatively identical to that of the corresponding bromo analog **A2**.

Anal. Calcd. for $C_{20}H_{20}ClNO_2$: C, 70.27; H, 5.89; N, 4.10; Cl, 10.38. Found: C, 70.14; H, 6.13; N, 4.21; Cl, 10.32.

cis-**5-Chloro-4-hydroxy-2-(*o*-hydroxyphenyl)-2-phenylvaleric Acid γ-Lactone (A6)**.—A solution of 1.5 g. (0.004 mole) of **A5** hydrochloride, m.p. 199–200°, in 15 ml. of 10% hydrochloric acid and 3 ml. of glacial acetic acid was heated on the steam bath for 5 hr. Cooling, collecting the product at the filter, and washing with water gave a crude product (1.1 g., 91%, m.p. 195–198°). Two recrystallizations from 95% ethanol gave pure **A6** (0.9 g.), m.p. 197–198° (m.m.p. with **A5** hydrochloride, 170–185°); $\lambda_{max}^{CHCl_3}$ (μ) 2.8 (w), 3.0–3.1 (w), 5.64 (m) (sh), 5.73 (s); λ_{max}^{Nujol} (μ) 2.99 (m), 5.71 (s). [This combination of bands and the effect on them of phase change (chloroform → Nujol) is, as indicated above under **A4** and **B4**, typical of the hydroxy lactone system common to all three compounds.][11]

Anal. Calcd. for $C_{17}H_{15}ClO_3$: C, 67.43; H, 4.99; Cl, 11.67; O, 15.85. Found: C, 67.33; H, 4.96; Cl, 11.43; O, 16.13.

3-Hydroxy-5-phenyl-2,3,4,5-tetrahydro-1-benzoxepin-5-carboxylic Acid γ-Lactone (V). A. From the Bridged Imidate IV.—A mixture of 30 g. (0.098 mole) of IV, 300 ml. of 10% hydrochloric acid, and 50 ml. of glacial acetic acid was stirred and refluxed for 16 hr. and then worked up as in the foregoing procedure. There was obtained 25.3 g. (97%) of crude lactone, m.p. 168–172°. Recrystallization of a sample from 95% ethanol gave pure V, m.p. 171–172°; $\lambda_{max}^{CHCl_3}$ (μ) 5.63 (s); $\lambda_{max}^{C_2H_5OH}$ (mμ) 265 (ε 760), 273 (ε 680); for the n.m.r. spectrum see Table I.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30; O, 18.03. Found: C, 76.67; H, 5.50; O, 17.83.

B. From the Bromo Lactone A4.—Treatment of 1.8 g. (0.0052 mole) of **A4** with an equivalent of sodium methoxide in 1,2-dimethoxyethane, exactly as described for the preparation of compound **B3**, gave 0.90 g. (65%) of the bridged lactone V, m.p. 169–170°, identical (infrared spectrum and mixture melting point) with the material prepared from the bridged imidate IV.

C. From the Chloro Lactone A6.—Likewise, 0.54 g. (0.00178 mole) of **A6**, treated with sodium methoxide in 1,2-dimethoxyethane in the usual way, gave 0.31 g. (65%) of the bridged lactone V, identical with the material obtained from IV.

Proton Magnetic Resonance Spectrum of the Bridged Lactone V.—The complex spectrum, peak assignments, and relative integrated areas (assuming 9 aromatic hydrogens) are summarized in Table I. It is apparent that the spectrum is consistent with the assigned structure.

TABLE I

Multiplet centers, τ	Assignment, *cf.* V	Relative area
2.25, 2.62, 2.94, 3.54	Aromatic H's	9 (assumed)
5.07	—CH—O—C=O	1
5.54, 5.94	—O—CH_2—C—O—C=O	2
7.05, 7.12	—C—CH_2—C—O—C=O	2

trans-**2-Hydroxymethyl-4-phenyl-4-chromancarboxylic Acid (A8)**.—Treatment of 3.5 g. (0.01 mole) of the *trans*-bromo lactone **B4** with an equivalent of sodium methoxide in 1,2-dimethoxyethane as described for the preparation of **B3** gave 1.4 g. of a glassy substance which could not be crystallized but whose infrared spectrum indicated that it was a hydroxy ester: $\lambda_{max}^{CHCl_3}$ (μ) 2.83 (OH), 5.80 (ester >C=O). This glass was refluxed in 15 ml. of 10% aqueous potassium hydroxide for 36 hr., cooled, extracted with ether to remove a little insoluble material, and acidified with concentrated hydrochloric acid. Isolation in the usual way gave the crude hydroxy acid (1.1 g., m.p. 170–175°), which was crystallized three times from a 2-butanone–pentane mixture to give pure **A8** (0.4 g.), m.p. 189–190°; λ_{max}^{Nujol} (μ), 2.99 (w) 5.88 (s).

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67; O, 22.51. Found: C, 72.01; H, 5.75; O, 22.39.

2-Hydroxy-2-methyl-4-phenyl-4-chromancarboxylic Acid γ-Lactone (VI) and A8 from the *trans*-Bromo Ester A1.—A suspension of 2.2 g. (0.006 mole) of methyl *trans*-2-bromomethyl-4-phenyl-4-chromancarboxylate (**A1**)[2] in 18 ml. of 10% aqueous potassium hydroxide was refluxed for 48 hr. The reaction mixture was worked up as in the foregoing procedure to obtain 1.7 g. of a glass which crystallized on trituration with aqueous methanol. Recrystallization from aqueous ethanol gave 0.5 g. (31%) of pure VI, m.p. 132–133°; $\lambda_{max}^{CHCl_3}$ (μ), 5.60 (s), no hydroxyl or carboxyl absorption; for the n.m.r. spectrum see Table II.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30; O, 18.03. Found: C, 76.40; H, 5.50; O, 17.75.

From the filtrate was obtained 0.5 g. (28%) of crude hydroxy acid **A8**, m.p. 180–184°. Two recrystallizations from a 2-butanone–pentane mixture gave 0.3 g. of pure **A8**, m.p. 189–190°, shown by elemental analysis, mixture melting point, and infrared spectrum to be identical with the sample prepared from the bromo lactone **B4**.

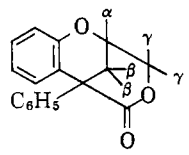
Proton Magnetic Resonance Spectrum of the Bridged Lactone VI.—Table II summarizes the data assuming that 9 aromatic hydrogens are present in the molecule.

TABLE II

Single peaks, τ	Assignment, *cf.* VI	Relative area
2.3–3.0	Aromatic H's	9 (assumed)
7.32	—C—CH_2—C—	2
8.08	CH_3	3

The occurrence of methyl absorption as a single peak is in accord with the assigned structure. However, the absence of

mutual spin–spin splitting by the methylene hydrogens is unexpected. Nevertheless, it is in line with the surprisingly simple spectrum of the following isomeric lactone.[2]



In this case, both β-CH_2 and γ-CH_2 absorptions occur as two doublets (J = 2.8 c.p.s.) centered at 7.63 and 5.37 τ, respectively, and the α-CH appears as a quintet (J = 2.8 c.p.s.) centered at 5.25 τ. This shows that neither the β-CH_2 nor the γ-CH_2 protons undergo appreciable mutual spin–spin splitting in this molecule.

cis-2-Hydroxymethyl-4-phenyl-4-chromancarboxylic Acid (B8). —A suspension of 1.8 g. (0.005 mole) of methyl *cis*-2-bromomethyl-4-phenyl-4-chromancarboxylate (B1)[2] in 15 ml. of 10% aqueous potassium hydroxide was refluxed for 64 hr. Isolation in the usual manner gave 1.2 g. (89%, m.p. 173–176°) of crude product which was recrystallized twice from aqueous ethanol to give pure *cis*-hydroxy acid B8 (0.77 g.), m.p. 176–177°; λ_{max}^{Nujol} (μ) 2.95 (w), 5.87 (s).

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67; O, 22.51. Found: C, 71.44; H, 5.79; O, 22.58.

Acknowledgment —Grateful appreciation is due Mr. W. H. Washburn for the infrared spectra; Dr. T. F. Page, Jr., Battelle Memorial Institute, Dr. R. W. Mattoon, and Dr. J. Tadanier for the n.m.r. spectra and for aid in their interpretation; and Mr. E. F. Shelberg and Mr. O. Kolsto for the microanalyses.

The Reaction of Oxalyl Chloride with Amides. II. Oxazolidinediones and Acyl Isocyanates

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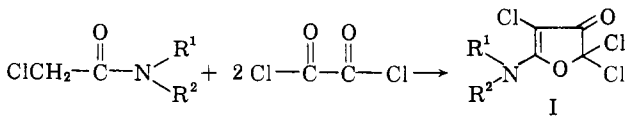
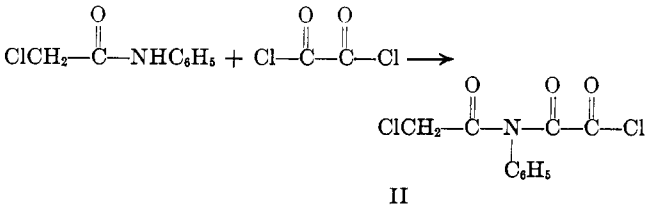
The reaction of oxalyl chloride with N-monosubstituted amides has been shown to yield acyloxamic acid chlorides or 2-methyleneoxazolidine-4,5-diones depending on the structure of the amide and experimental conditions. Treatment of primary amides with oxalyl chloride was found to be a general preparation of acyl isocyanates. A mechanism for the reaction of oxalyl chloride with various amides is discussed.

The reaction of oxalyl chloride with N,N-disubstituted chloroacetamides has been shown to yield trichlorofuranone amines I.[1]



I

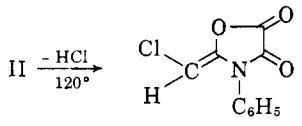
Since the formation of furanone amines would be very unlikely from N-monosubstituted chloroacetamides and oxalyl chloride, it was of interest to determine the course of this reaction. Interaction of α-chloroacetanilide and oxalyl chloride in carbon tetrachloride at 60° for twenty-four hours led to the isolation of N-chloroacetyloxanilic acid chloride (II).



II

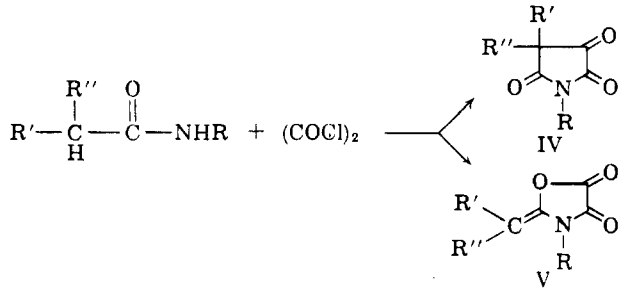
It exhibited carbonyl absorption at 1855, 1840, and 1765 cm.$^{-1}$ (Nujol) but none in the NH region. Treatment of II with methanol gave methyl N-chloroacetyl oxanilate which absorbed in the infrared at 1768, 1748, and 1720 cm.$^{-1}$ (chloroform). N.m.r. spectrum of the ester showed the presence of five protons with a complex aromatic absorption centered at 2.55 τ, two protons in a singlet at 5.90 τ, and three protons in a singlet at 6.11 τ.

On heating II at 120° for 5 min., hydrogen chloride was evolved and III was isolated. III had infrared absorption at 1827, 1745, and 1682 cm.$^{-1}$ (Nujol) with bands indicative of a vinyl proton at 3100 and 862 cm.$^{-1}$. Ultraviolet maxima were found at 235 mμ (log ϵ 3.62) and 300 mμ (log ϵ 3.82). Its n.m.r. spectrum showed the five aromatic protons centered at 2.43 τ and a singlet, perhaps due to a vinyl proton, at 4.75 τ. On the basis of the foregoing data, the structure of the compound is formulated as 2-chloromethylene-3-phenyloxazolidine-4,5-dione (III).



III

The reaction of oxalyl chloride with N-monosubstituted acetamide derivatives has led to some controversy. Figee[2] first reported that the products were pyrrolidinetriones IV without apparent justification or consideration of isomeric structures. Since the product from the reaction of oxalyl chloride and acetanilide was easily hydrolyzed to acetic acid and oxanilic acid, Stolle and Luther[3] considered the product to be the



IV

V

(1) A. J. Speziale and L. R. Smith, *J. Org. Chem.*, **27**, 4361 (1962).

(2) T. Figee, *Rec. trav. chim.*, **34**, 289 (1915).

(3) R. Stolle and M. Luther, *Ber.*, **53**, 314 (1920).