Dry Ice, whereupon a solid separated. The liquid layer was removed, fresh solvent was added, and the material again cooled in Dry Ice. The solid obtained in this way was dried *in vacuo* at room temperature, and then stored in the cold for several days. The product, thick white needles, m.p. 0–5° (approximate), slowly decomposed unless refrigerated.

Anal. Calcd. for $C_{12}H_{13}OCl$: C, 69.23; H, 6.25; Cl, 16.83. Found: C, 68.95; H, 6.53; Cl, 17.28.

1-Bromo-1-benzoylcyclopentane.—To 7.0 g. of benzoylcyclopentane dissolved in 70 ml. of dry ether, 7 g. of bromine was added gradually with stirring. After the addition was complete the reaction mixture was kept in a water-bath at 50° for 30 minutes. All solvent was then removed, and the residue was dried *in vacuo*. The yellow oil thus obtained was dissolved in 10 ml. of petroleum ether (65–70°) and allowed to crystallize in the cold. After two days of refrigeration, 7.0 g. (40%) of white crystalline material separated, m.p. 28–29.5°.

Anal. Calcd. for $C_{12}H_{13}OBr$: C, 56.92; H, 5.13; Br, 31.62. Found: C, 57.03; H, 5.13; Br, 31.68.

The Action of Sodium Methoxide on 1-Bromo-1,4-dibenzoylbutane.—To 1.5 g. (0.004 mole) of 1-bromo-1,4-dibenzoylbutane dissolved in 50 ml. of absolute ethanol was added 0.22 g. (0.004 mole) of sodium methoxide. The reaction mixture was left overnight at room temperature. The white needle-like precipitate, 0.4 g. (50%), which formed was filtered, washed with water and dried. After two recrystallizations from ethyl acetate this material melted at 165–166° and was identified as 1-phenyl-5-benzoyl-1-cyclopentene oxide by mixture melting point and comparison of infrared spectra. From the mother liquors was obtained 0.75 g. of starting material.

NEW HAVEN, CONN.

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

γ-Keto- and γ-Hydroxy-γ-phenylbutyramides. Synthesis, Absorption Spectra and Structure Studies

BY NORMAN H. CROMWELL AND KENNETH E. COOK[1]

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The reactions of amines with γ-phenyl-γ-butyrolactone have been shown to produce γ-hydroxy-γ-phenylbutyramides. α-Morpholino-γ-phenyl-γ-butyrolactone has been found to be resistant to ring opening by *sec*-amines, while benzylamine and cyclohexylamine react to produce the corresponding amides of α-morpholino-γ-hydroxy-γ-phenylbutyric acid. Several amides of β-benzoylpropionic acid have been prepared from the reactions of primary and secondary amines with γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide. The absorption spectra of these various products are discussed in connection with their structures and ring–chain tautomerism.

The reactions of γ-lactones with such unsymmetrical reagents as ammonia and amines have not been studied thoroughly. The two possible products would be γ-amino acids or γ-hydroxy amides.[2] If the usual ester reaction mechanism is followed, the main product should be the hydroxy amide.

The reaction between γ-phenyl-γ-butyrolactone and ammonia has been reported to give γ-hydroxy-γ-phenylbutyramide.[3,4] In a previous report[5] it was suggested that γ-phenyl-γ-butyrolactone reacts with morpholine to produce γ-morpholino-γ-phenylbutyric acid. This conclusion was based partly on the fact that the product dissolved in dilute sodium carbonate and in dilute acid. Moreover, this compound I produced morpholine hydrochloride on treatment with hydrogen chloride gas in dry ether solution. It has now been found that the other product from this treatment with hydrogen chloride is γ-phenyl-γ-butyrolactone. These properties seemed plausible for the γ-amino acid structure. From our subsequent studies, however, it now seems highly probable that this product is actually γ-hydroxy-γ-phenylbutyromorpholide (I).

The Nujol mull infrared spectrum of I was reported[5] to show a band at 3430 cm.$^{-1}$ which was assigned to an $\overset{+}{N}H$ absorption, but this seems to be high compared to the normal $\overset{+}{N}H_3$ absorption which is usually in the 3030–3130 cm.$^{-1}$ region.[6] The 3430 cm.$^{-1}$ band seems to be better suited to an associated OH absorption. An absorption band also appeared at 1618 cm.$^{-1}$ which was previously[5] assigned to the carboxylate ion absorption. However, the amide carbonyl absorption may also occur in this region although this is at the lower limit.

Subsequent reactions between γ-phenyl-γ-butyrolactone and piperidine, dimethylamine, benzylamine and cyclohexylamine have given products (II, III, IV and V) which also show infrared bands in the OH and amide carbonyl regions (see Table I). The greatly increased solubility of some of these compounds in ether strongly suggested that they did not have an amino acid structure. Infrared spectra studies of solutions of two of these compounds cleared up any doubts as to their correct structures. These later solution spectra studies showed that the OH and amide carbonyl bands were shifted to higher frequencies from the solid state data. The relatively low carbonyl and OH infrared bands for these compounds I–V suggests considerable hydroxyl–carbonyl hydrogen bonding in these γ-hydroxy amide structures.

The catalytic hydrogenation of N-cyclohexyl-γ-hydroxy-γ-phenylbutyramide (III), prepared from the reaction of γ-phenyl-γ-butyrolactone and cyclohexylamine, produced N-cyclohexyl-γ-phenylbutyramide, identical with a sample prepared from γ-phenylbutyryl chloride. This result supported

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[1] Monsanto Chemical Co. Research Fellow, 1956–1957.

[2] C. D. Lunsford, R. S. Murphey and E. K. Rose, *J. Org. Chem.*, **22**, 1225 (1957), report that γ-butyrolactone reacts with amines to produce γ-hydroxybutyramides and some γ-aminobutyric acid, and suggest that the latter product may be in equilibrium with the former. Chemical evidence for the presence of γ-aminobutyric acid in the reaction mixture was presented.

[3] R. Fittig and L. S. Morris, *Ann.*, **256**, 156 (1889).

[4] R. R. Russell and C. A. VanderWerf, THIS JOURNAL, **69**, 11 (1947).

[5] N. H. Cromwell, P. L. Creger and K. E. Cook, *ibid.*, **78**, 4412 (1956).

[6] L. J. Bellamy, "Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954.

the assignment of the N-cyclohexyl-γ-hydroxy-γ-phenylbutyramide structure to compound III.

With the hope of preparing a series of α-amino-γ-hydroxy-γ-phenyl-butyramides for pharmacological testing, the reaction of the known α-morpholino-γ-phenyl-γ-butyrolactone[5] with amines was investigated. This lactone ring proved to be difficult to open on treatment with secondary amines, or with acids. However, both cyclohexylamine and benzylamine reacted on heating to produce the corresponding N-cyclohexyl- and N-benzyl-α-morpholino-γ-hydroxy-γ-phenylbutyramides (VI) and (VII).

On heating α-morpholino-γ-phenyl-γ-butyrolactone with aqueous methylamine or aqueous ammonia, α-morpholino-γ-hydroxy-γ-phenylbutyric acid (VIII) was produced. The infrared spectra of VI and VII showed OH, NH and amide C=O bands in the expected regions of the spectrum, while VIII showed the OH, NH and an ionized CO_2^- band; see Table I.

TABLE I

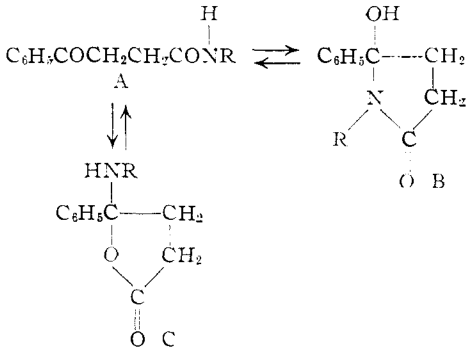
SUMMARY OF INFRARED SPECTRA FOR DERIVATIVES OF γ-HYDROXY-γ-PHENYLBUTYRIC ACID, $C_6H_5CH(OH)CH_2CH(R')COR$

				Wave no. cm.$^{-1}$		
No.	R	R′	Band assign.	ν, Nujol mull	ν, soln.	% abs.
I	NC_4H_8O[a]	H	OH	3430	...	..
			Amide C=O	1617	...	..
			Phenyl	1588	...	..
II	NC_5H_{10}	H	OH	3412	...	..
			Amide C=O	1622	...	..
			Phenyl	1587	...	..
V	$N(CH_3)_2$	H	OH	3400	...	..
			Amide C=O	1630	...	..
			Phenyl	1603	...	..
IV	$HNCH_2C_6H_5$	H	OH	3396	3440[b]	80
			NH	3335	3350	85
			Amide C=O	1648	1677	100
			Phenyl	1608	1605	40
			Amide II	1552	...	..
III	$HN-C_6H_{11}$	H	OH	3265	3610[c]	15
			NH	3080	3430	25
			Amide C=O	1625	1660	50
			Phenyl	1582	...	..
VII	$HNCH_2C_6H_5$	NC_4H_8O	OH	3345	...	..
			NH	3250	...	..
			Amide C=O	1643	...	..
			Phenyl	1605	...	..
			Amide II	1540	...	..
VI	HNC_6H_{11}	NC_4H_8O	OH	3285	...	..
			NH	3150	...	..
			Amide C=O	1642	...	..
			Phenyl	1603	...	..
			Amide II	1560	...	..
VIII	OH	NC_4H_8O	OH	3450	...	..
			^+NH	3250	...	..
			Ionized CO_2^-	1612	...	..

[a] Values from ref. 5 with new band assignments. [b] 18.5 mg./ml. in dioxane, NaCl prisms; 1-mm. NaCl cells. [c] Satd. soln. in CCl_4, Li–F prisms; 1-mm. NaCl cells.

When α-morpholino-γ-phenyl-γ-butyrolactone was refluxed with concd. hydrochloric acid only the known[5] hydrochloride IX of the starting amino lactone was isolated.

β-Benzoylpropionamides and Ring–Chain Tautomerism.—In a previous investigation[5] it was found that morpholine reacts with γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide in dry ether at room temperature to produce β-benzoylpropionmorpholide. It has been reported by others[7] that when ammonia and amines react with lactones such as γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide, the primary products formed are open chain amides like β-benzoylpropionamides. When ammonia or a primary amine is used the primary product, the β-benzoylpropionamide (A), might undergo a ring closure to produce the isomeric 5-hydroxy-5-phenylpyrrolidinone-2 (B) or the 5-amino-5-phenylbutyrolactone (C).



Walton[8] reported that several amines reacted with the butenolide to give crystalline products. Most of his products were amphoteric, dissolving in 6 *N* hydrochloric acid and 2 *N* sodium hydroxide. Several of these compounds were reported to be remarkably stable in alkali but to be decomposed with hydrochloric acid into β-benzoylpropionic acid and the corresponding amine. Walton interpreted these facts as pointing to the pyrrolidinone structure B for his products.

It seemed important that this type of ring–chain tautomerism be studied by modern diagnostic spectroscopic methods to decide, if possible, the structures of these materials in both the solid and solution states. The reactions of γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide with various amines are described in the Experimental section and the ultraviolet and infrared spectra of the products are recorded in Table II.

The infrared spectra of the β-benzoylpropionamides (tautomers A) would be expected[6] to show distinct benzoyl and amide carbonyl bands, an NH stretching band and an amide II band, whereas the spectra of the hydroxypyrrolidinones (tautomers B) should show a carbonyl band characteristic of 5-membered ring cyclic amides and an OH stretching band. The amino lactones C should show lactone carbonyl bonds. The ultraviolet spectra of β-benzoylpropiondiimides should show a distinctive absorption due to the benzoyl resonance which would be lacking in the hydroxypyrrolidinones (tautomers B) or amino lactones C.

An examination of the infrared data recorded in Table II indicates that all of the compounds listed, except the reaction product of methylamine with the butenolide, are β-benzoylpropionamides in the solid state. The Nujol mull spectra show benzoyl carbonyl bands between 1686 and 1673 cm.$^{-1}$ and amide carbonyl bands between 1625 and 1655 cm.$^{-1}$. The aniline derivative and amides X and XI

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[7] (a) L. Wolff, *Ann.*, **229**, 256 (1885); (b) J. Biedermann, *Ber.*, **24**, 4077 (1891); (c) L. Lukes and V. Prelog, *Coll. Czech. Chem. Comm.*, **1**, 119, 287, 334, 461, 617 (1929).

[8] E. Walton, *J. Chem. Soc.*, 438 (1940)

TABLE II

SUMMARY OF ULTRAVIOLET AND INFRARED SPECTRA OF β-BENZOYLPROPIONAMIDES, $C_6H_5COCH_2CH_2CON<$

		Ultraviolet max.[a]			Infrared bands[b]		
N<	No.	λ, mμ	$\epsilon \times 10^{-3}$	Band	Nujol γ, cm.$^{-1}$	Sol. γ, cm.$^{-1}$	% abs.
NH_2	..	242	13.2	OH/NH	3350[c]	3440[d]	30
		280	1.2		3172	3350	32
				Keto C=O	1675	1687	93
				Amide C=O	1625	1620	26
				Phenyl	1594	1600	30
$NHCH_3$	..	240	0.77	OH/NH	...	(3560)[f]	50
					3230[c]	3390	83
		(256)[e]	0.43	Amide C=O	1687	1683[g]	81
		(262)	.25		1677	1680	
		(265)	.15	Amide II	None	None	
		278	.09	Phenyl	None	None	
NHC_6H_5	..	243	26.4	OH/NH	...	3480[h]	5
		280	3.6		3300[c]	3310	18
				Keto C=O	1676	1683[i]	64
				Amide C=O	1655		
				Phenyl	1693	1600	45
				Amide II	1535	1536	41
$NHCH_2C_6H_5$	X	240	12.5	OH/NH	3310[c]	3500[h]	10
		277	1.1		3272	3350	23
				Keto C=O	1682	1675[c]	73
				Amide C=O	1628		
				Phenyl	...	1600	17
				Amide II	1550	1530	39
NHC_6H_{11}	XI	240	13.3	OH/NH	...	3570[h]	23
					...	3500	20
		279	1.8		3325[c]	3360	20
				Keto C=O	1683	(1685)[j]	50
				Amide C=O	1628	1672	68
				Phenyl	1600	1600	16
				Amide II	1550	1530	43
NC_4H_8O[k]	..	242	15.0	Keto C=O	1686	1685	50
		280	1.3	Amide C=O	1643	1653	70
				Phenyl	1598	1600	15
$N(CH_3)_2$	XII	..	...	Keto C=O	1681	1685[l]	92
				Amide C=O	1645	1655	90
				Phenyl	1597	(1638)	85
						(1600)	50
$N(CH_3)CH_2C_6H_5$	XIII	..	...	Keto C=O	1673	1685[l]	92
				Amide C=O	1640	1652	89
				Phenyl	1595	(1638)	85
						(1600)	40

[a] All ultraviolet spectra were determined at 25° with a Cary recording spectrophotometer model 11 MS, using 95% ethanol solutions. [b] Infrared spectra were determined between 700 and 4000 cm.$^{-1}$ with a Perkin–Elmer model 21 double beam infrared spectrophotometer using NaCl optics unless otherwise indicated. [c] LiF optics were used. [d] Using a 18.5 mg./ml. dioxane solution and 0.1-mm.-matched cells. [e] Values in parentheses indicate inflections or shoulders. [f] Using 12.5 mg./ml. dioxane solutions and 1.0-mm. cells. [g] Broad band; a satd. CCl_4 sol. showed C=O bands at 1705 and 1677 cm.$^{-1}$ and weak OH and/or NH bands at 3595 and 3210 cm.^{1} (broad). [h] Using 25 mg./ml. dioxane solutions and 0.1-mm. cells. [i] In a satd. CCl_4 soln. the C=O band was found at 1687 cm.$^{-1}$, and an NH or OH band at 3440 cm.$^{-1}$, using LiF optics. [j] In a satd. CCl_4 soln. the C=O bands were found at 1685 and 1675 cm.$^{-1}$ and OH and/or NH bands at 3430, 3380 and 3340 cm.$^{-1}$ using LiF optics. [k] See ref. 5 for infrared values; infrared soln. values were obtained using 0.1-mm. cells and a concn. of 20 mg./ml. CCl_4. [l] Using 25 mg./ml. CCl_4, LiF optics and 1.0-mm. NaCl cells.

showed amide II bands at 1535–1550 cm.$^{-1}$. The NH stretching vibration bands for these primary amine derivatives are apparently those appearing between 3172 and 3350 cm.$^{-1}$ in the solid state spectra.

Solution infrared data for these materials were difficult to obtain because of the low solubility of the compounds in desirable solvents (*i. e.*, CCl_4). Using dioxane solutions the infrared spectra of all of the primary amine derivatives, but not the ammonia derivative, showed a strong, broad, poorly resolved carbonyl band between 1672 and 1685 cm.$^{-1}$. These spectra all had rather complex bands in the OH and NH stretching region between 3560 and 3310 cm.$^{-1}$. The dioxane solution spectra for the aniline derivatives and compounds X and XI also appeared to have amide II bands. It seems evident that in dioxane solution the methylamine, aniline, benzylamine (X) and cyclohexylamine (XI) reaction products with γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide exist as tautomeric mixtures ($A \rightleftarrows B$) of the β-benzoylpropionamide and the 5-hydroxy-5-phenylpyrrolidinone-2. The infrared spectrum of the ammonia derivative in dioxane indicates that it exists in this solvent mainly as β-benzoylpropionamide, showing a benzoyl carbonyl band at

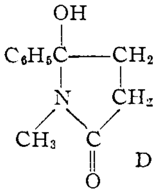
1687 cm.$^{-1}$, an amide carbonyl band at 1620 cm.$^{-1}$, and a well defined conjugated phenyl band at 1600 cm.$^{-1}$.

In both the solid and solution states the methylamine derivative showed infrared carbonyl bands in the range of 1677–1687 cm.$^{-1}$ which seem to be too high for an amide carbonyl band of an open chain N-methylamide, but not too high for a five-membered ring lactam[6] (pyrrolidinone, tautomer B). Moreover, this methylamine derivative's infrared spectra showed neither an amide II band nor a conjugated phenyl band which would be expected for N-methyl-β-benzoylpropionamide (tautomer A).

The infrared spectra of the secondary amine derivatives of γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide indicate that the morpholine derivative and compounds XII and XIII are N,N-disubstituted-β-benzoylpropionamides. These three substances have well defined, symmetrical benzoyl carbonyl bands at 1685 cm.$^{-1}$ and amide carbonyl bands at 1652–1653 cm.$^{-1}$ in their carbon tetrachloride solution spectra, and at 1673–1686 cm.$^{-1}$ and 1640–1645 cm.$^{-1}$, respectively, in their Nujol mull spectra.

The ultraviolet spectra measured for some of these butenolide derivatives were particularly instructive. Thus the ammonia, the aniline, the morpholine, the benzylamine (X) and cyclohexylamine (XI) derivatives all showed strong benzoyl absorption with maxima at λ 240–243 mμ (ε 12,500–26,400). In 95% ethanol solution it seems certain that these compounds exist mainly as β-benzoylpropionamides (tautomer A).

Only weak benzoyl absorption was indicated in the spectrum of the methylamine derivative (λ 240 mμ, ε 770) and so it seems evident that this compound exists mainly as 1-methyl-5-hydroxyl-5-phenylpyrrolidinone (D), as suggested by Walton.[8]



D

Acknowledgment.—This investigation was supported in part by a grant from the National Cancer Institute, U. S. Public Health Service, CY2931.

Experimental

Reaction of γ-Phenyl-γ-butyrolactone with Amines.—Equimolar amounts of γ-phenyl-γ-butyrolactone and the amines (morpholine, piperidine, cyclohexylamine and benzylamine) were dissolved in tech. grade ether and allowed to stand at room temperature for two to four days. Cooling the solutions gave solid products which were recrystallized from a mixture of benzene and petroleum ether (b.p. 60–70°). Similar reaction conditions employing diethylamine, N-methylbenzylamine or N-methylpiperazine produced oils which resisted crystallization.

γ-Hydroxy-γ-phenylbutyromorpholide (I), m.p. 93–95°, yield 85%. This product previously was assigned the incorrect structure, γ-phenyl-γ-morpholinobutyric acid.[5] Compound I dissolved on standing in dilute sodium carbonate or in dilute hydrochloric acid solutions. On treating an ether solution of I with dry hydrogen chloride gas, morpholine hydrochloride, m.p. 176–177°, was precipitated. The ether solution was washed with water, dried and concentrated to produce γ-phenylbutyrolactone, m.p. 43–45°.[4]

γ-Hydroxy-γ-phenylbutyropiperidide (II), m.p. 37–38°, yield 33%. When this material was mixed with the starting lactone an oil was produced.

Anal. Calcd. for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.76; H, 8.72; N, 5.56.

N-Cyclohexyl-γ-hydroxy-γ-phenylbutyramide (III), m.p. 90–92°, yield 88%. This compound was insoluble in 0.1 *N* sodium hydroxide or in 3.0 *N* hydrochloric acid.

Anal. Calcd. for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.55; H, 8.90; N, 5.55.

N-Benzyl-γ-hydroxy-γ-phenylbutyramide (IV), m.p. 93–94°, yield 92%. This product was insoluble in 0.1 *N* sodium hydroxide or in 3 *N* hydrochloric acid.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found C, 75.95; H, 7.00; N, 4.81.

N,N-Dimethyl-γ-hydroxy-γ-phenylbutyramide (V).—A 0.5-g. sample of γ-phenyl-γ-butyrolactone and 1.5 ml. of an aqueous 25% solution of dimethylamine were heated in a sealed tube at 70° for four hours. Evaporation of the reaction mixture to dryness and recrystallization of the residue from ether and petroleum ether resulted in a 27% yield of the colorless product, m.p. 56–57°.

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.64; H, 8.34; N, 6.71.

Reactions of α-Morpholino-γ-phenyl-γ-butyrolactone. N-Cyclohexyl- and N-Benzyl-α-morpholino-γ-hydroxy-γ-phenylbutyramide (VI) and (VII).—Two gram samples of α-morpholino-γ-phenyl-γ-butyrolactone[5] and 2 ml. of the amines (cyclohexylamine and benzylamine) were heated under reflux for 6 hr. The cooled reaction mixtures were dissolved in ether, washed with water and dried. Concentration of these ether solutions and dilution with petroleum ether produced the materials which were recrystallized from benzene and petroleum ether. Amide VI was produced in 36% yield, m.p. 128–130°.

Anal. Calcd. for $C_{20}H_{30}N_2O_3$: C, 69.33; H, 8.73; N, 8.09. Found: C, 69.13; H, 8.69; N, 8.20.

Amide VII was obtained in a 63% yield, m.p. 139–141°.

Anal. Calcd. for $C_{21}H_{26}N_2O_3$: C, 71.16; H, 7.39; N, 7.90. Found: C, 71.18; H, 7.43; N, 7.97.

α-Morpholino-γ-hydroxy-γ-phenylbutyric Acid (VIII).—A 0.5-g. sample of α-morpholino-γ-phenyl-γ-butyrolactone[5] and 1 ml. of an aqueous 25% solution of dimethylamine were heated in a sealed tube at 75° for 3 hr. The reaction mixture was evaporated to dryness and the residue recrystallized from ethanol to give a 93% yield of VIII, m.p. 167–170°. A sealed tube reaction using concd. ammonium hydroxide produced the same compound in 78% yield.

Anal. Calcd. for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.70; H, 7.14; N, 5.31.

α-Morpholino-γ-phenyl-γ-butyrolactone Hydrochloride (IX).—A 1.0-g. sample of the amino lactone was heated under reflux with 5 ml. of concd. hydrochloric acid for one hour. Cooling the reaction mixture produced IX which was identical with a sample formed by passing dry hydrogen chloride gas into an ether solution of the amino lactone. Recrystallized from methanol and ether, this compound showed m.p. 243° (lit.[5] m.p. 230°); infrared spectrum, $\gamma_{C=O}$, 1780 cm.$^{-1}$ (Li-F prisms, hexachlorobutadiene mull).

With *sec*-amines (morpholine, piperidine, anhyd. dimethylamine and N-methylpiperizine) α-morpholino-γ-phenyl-γ-butyrolactone on heating gave only oils which did not crystallize, and in some cases starting material was recovered. On standing at room temperature with an ether solution of morpholine or piperidine the α-morpholino-γ-phenyl-γ-butyrolactone was recovered unchanged.

Reaction of γ-Phenyl-$\Delta^{\beta,\gamma}$-butenolide with Amines. β-Benzoylpropionamide, N-methyl-β-benzoylpropionamide and N-phenyl-β-benzoylpropionamide were prepared from γ-phenyl-$\Delta^{\beta,\gamma}$-butenolide and ammonia, methylamine and aniline, respectively, following the directions of Walton.[8]

γ-Phenyl-$\Delta^{\beta,\gamma}$-butenolide was allowed to react with an excess of several amines in tech. grade ether solutions which were allowed to stand at room temperature for a week. Evaporation of the solvent and recrystallization of the residues furnished the colorless, crystalline products.

N-Benzyl-β-benzoylpropionamide (X), m.p. 110–111°, 80% yield, recrystallized from 95% ethanol. *Anal.* Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.70; H, 6.46; N, 5.27.

N-Cyclohexyl-β-benzoylpropionamide (XI), m.p. 109–111°, yield 50%, recrystallized from aq. ethanol. *Anal.* Calcd. for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.33; H, 7.79; H, 5.06.

N,N-Dimethyl-β-benzoylpropionamide (XII), m.p. 55–55.5°, recrystallized from ether; yield 69%. *Anal.* Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.49; H, 7.37; N, 6.93.

N-Benzyl-N-methyl-β-benzoylpropionamide (XIII), m.p. 68–70°, recrystallized from benzene–petroleum ether; yield 98%. *Anal.* Calcd. for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 77.00; H, 6.69; N, 4.93.

N-Cyclohexyl-γ-phenylbutyramide.—a. A 0.5-g. sample of III was dissolved in 25 ml. of methanol and shaken under 45 lb./in.² pressure of hydrogen in the presence of 10% Pd-on-charcoal catalyst. The product was recrystallized from ether, m.p. 91–92°; infrared spectrum, $\gamma_{C=O}$, 1675 cm.$^{-1}$; γ_{N-H}, 3440 cm.$^{-1}$ (CCl_4 soln.).

Anal. Calcd. for $C_{16}H_{23}NO$: C, 78.30; H, 9.45; N, 5.71. Found: C, 78.45; H, 9.42; N, 5.79.

b. This amide also was prepared from γ-phenylbutyric acid *via* the acid chloride in 53% yield according to the method previously outlined for γ-phenylbutyromorpholide.[5]

LINCOLN, NEBR.

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Sodium β-Formyl-β-keto-α-nitropropionate from the Reaction of Mucochloric Acid with Sodium Nitrite[1]

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Sodium β-formyl-β-keto-α-nitropropionate (III) has been isolated from the reaction of mucochloric acid with sodium nitrite in aqueous alcohol at 35°. Evidence for the structure of III was obtained by reaction with phenylhydrazine to give a stable phenylosazone and reaction with *o*-phenylenediamine to give 2-nitromethylquinoxaline, which was oxidized to the known quinoxaline-2-carboxylic acid.

The reaction of mucobromic acid (Id, *cis*-α,β-dibromo-β-formylacrylic acid) with metal nitrites was studied many years ago by Hill and his students,[2] who reported in a series of papers the isolation and characterization of sodium nitromalonaldehyde (IV), several other salts of nitromalonaldehyde and the dipotassium salt of α,α,β-trinitropropionaldehyde (VI). No other products have been isolated from the reaction of the mucohalic acids (Ia-d) with nitrite.

The usefulness of sodium nitromalonaldehyde as an intermediate in synthetic organic chemistry[3] later stimulated a search for a cheaper and more efficient method of preparation. A summary of the studies of the preparation of nitromalonaldehyde by the reaction of the mucohalic acids is presented in Table I. Although the yields reported by different authors disagree somewhat, it is evident from these data that the acids which have β-bromo atoms (Ib and d) give significantly higher yields than the acids which have β-chloro atoms (Ia and c).

TABLE I

Mucohalic acid treated with sodium nitrite in aq. alcohol at 54–60°, β-formylacrylic acid	Yield of sodium nitromalonaldehyde claimed, %
Ia, *cis*-α,β-Dichloro-	"Very small,"[4] 13[5,8]
Ib, *cis*-β-Bromo-α-chloro-	26,[5] 43[6]
Ic, *cis*-α-Bromo-β-chloro-	"Low"[4]
Id, *cis*-α,β-Dibromo-	41,[7] 35[5]

Although mucochloric acid (Ia) reacts readily with sodium nitrite in aqueous alcohol and the starting material is not recoverable, previous reports of this reaction have accounted for only a very small fraction of the starting material in the form of the product sodium nitromalonaldehyde.

In the present paper we describe the isolation and characterization of a new compound, sodium β-formyl-β-keto-α-nitropropionate (III), from the reaction of mucochloric acid with sodium nitrite, and discuss the significance of this observation with regard to a rational mechanism for the reaction of the mucohalic acids with nitrite.

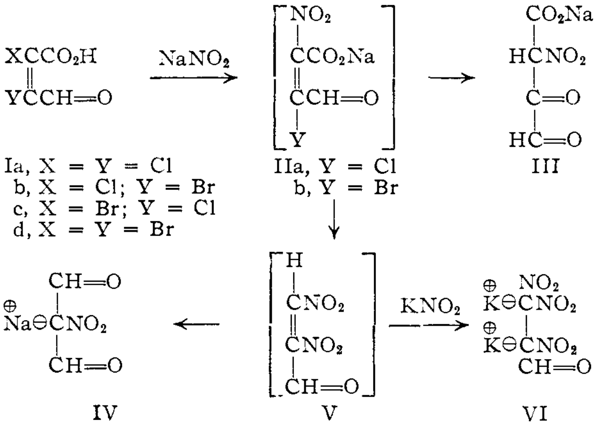

Fig. 1.—Condensed scheme for the reactions of the mucohalic acids with nitrite. Hypothetical intermediates are in brackets.

From the reaction of mucochloric acid with sodium nitrite in dilute alcohol at 35°, a white solid was obtained which had no definite melting point below 300°, and exploded when heated on a spatula over an open flame. Analysis of the material was in agreement with the formula $C_4H_2NO_6Na \cdot 2H_2O$ and the infrared absorption spectrum in a Nujol

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[2] (a) H. B. Hill and J. Torrey, *Am. Chem. J.*, **22**, 89 (1899); (b) J. Torrey and O. F. Black, *ibid.*, **24**, 452 (1900).

[3] The literature has been surveyed by R. A. Stein, Ph.D. Thesis, Illinois Institute of Technology, June, 1955.

[4] E. Kuh and R. L. Shepard, THIS JOURNAL, **75**, 4597 (1953).

[5] C. C. Price and T. L. V. Ulbricht, *J. Org. Chem.*, **22**, 235 (1957).

[6] E. Kuh and H. W. Steward, U. S. Patent 2,606,931 (Aug. 12, 1952).

[7] P. E. Fanta, *Org. Syntheses*, **32**, 95 (1952).

[8] Dr. C. Stuckwisch reported in a private communication to the author that a better yield of nitromalonaldehyde was obtained from mucochloric acid by operating at 45–50°, according to directions appearing in the Ph.D. Thesis of N. M. Sandberg, University of Wichita.