The burets were of the automatic-zero type with integral reservoirs; they were filled by nitrogen pressure and protected by drying tubes filled with Ascarite. One buret (25 ml) delivered carbon dioxide-free ethanol, and one buret (5 ml) delivered aqueous carbonate-free sodium hydroxide. The electrodes were Fisher No. 13-639-12 (glass) and No. 13-639-52 (calomel); a Beckman Model G pH meter was used for the titrations. The nitrogen was passed through two gas washing bottles filled with 50% aqueous ethanol, and the titration vessel was covered with a sheet of parafilm.

Procedure.—A sample of the acid (about 0.33 mmol) was placed in the titration vessel and dissolved in 25 ml of ethanol, with stirring. Carbon dioxide-free water (25 ml) was pipetted in, and the solution allowed to come to thermal equilibrium (10–15 min). The initial pH reading was taken and a 0.5-ml aliquot of 0.02 *N* sodium hydroxide was added, followed by a 0.5-ml aliquot of ethanol. The mixture was stirred for 30 sec and allowed to stand for 15 sec, and the pH reading was taken. About 30 readings per run were taken in this manner, up to pH 11. Nitrogen flow was maintained throughout the run.

Solutions.—Carbon dioxide-free distilled water was prepared by boiling distilled water for 5 min, stoppering the flask, and allowing it to cool. Carbon dioxide-free ethanol was prepared by bubbling dry nitrogen through absolute ethanol for 20–30 min.

Carbonate-free sodium hydroxide was prepared by dissolving reagent grade sodium hydroxide (4 g) in 4 ml of carbon dioxide-free water and allowing to stand. A 1.1-ml portion of the supernatant 50% solution was diluted to 1 l., which was approximately 0.02 *N*. The solution was standardized against potassium hydrogen phthalate with phenolphthalein indicator.

The pH 4.00 buffer (25°) was prepared by dissolving 10.2114 g (0.05 mol) of potassium hydrogen phthalate in 1 l. of carbon dioxide-free water. The pH 9.18 buffer (25°) was prepared by dissolving 19.0687 g (0.05 mol) of sodium borate decahydrate (borax) in 1 l. of carbon dioxide-free water.

Calculations.[66]—The pK_a values were calculated at each point and corrected for H^+ activity below pH 7 and for OH^- activity above pH 7. The following equations were used.

pH 0-7 $pK_a = pH + [(HA) - (H^+)] - \log [(A^-) + (H^+)]$

pH 7 $pK_a = pH + \log (HA) - \log (A^-)$

pH 7-14 $pK_a = pH + \log [(HA) + (OH^-)] - \log [(A^-) - (OH^-)]$

The activity corrections were assumed to be the same for 50% ethanol as for water; the constant pK_a values obtained support this assumption. It was also assumed that the pH reading was equal to the logarithm of the reciprocal of the hydrogen ion concentration; no correction was made for the liquid-junction potential.

The pK_a values were converted to K_a values, averaged, and reconverted to an average pK_a. The pK_a value with the largest deviation from the average was discarded, and a new average pK_a determined. The process was repeated until the largest deviation was less than 0.03 pH unit. The calculations were performed on an IBM 1130 computer. The values are presented in Table XI.

Registry No.—β-*d*-Carbethoxycyclooctane, 26600-46-4; β-*d*-cyclooctylcarbinol, 26600-47-5; β-*d*-cyclooctylcarbinyl tosylate, 26600-48-6; cycloalkylcarbinyl acetate (5 ring size), 26600-49-7.

Acknowledgment.—The authors wish to thank the National Science Foundation (GP-9248) for financial support.

(66) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Wiley, New York, N. Y., 1962.

The Chemistry of Acylsalicylamides. I. The Base-Catalyzed Decomposition of *O*-Benzyloxycarbonylglycyl-*N*-ethylsalicylamide

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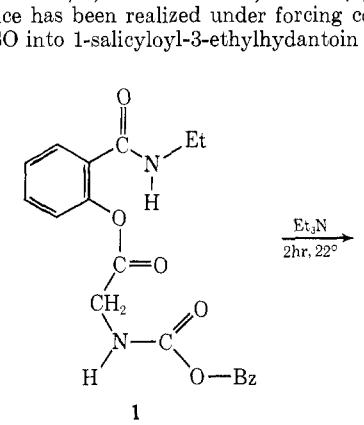
The structure of the major product obtained when *O*-benzyloxycarbonylglycyl-*N*-ethylsalicylamide (**1**) is treated with triethylamine is shown to be 3-(*N*-ethylacetamido)-1,3-benzoxazine-2,4-dione (**3**). The extensive ring–chain tautomerism potentially open to this substance has been realized under forcing conditions by conversion of **3** upon treatment with dimsyl sodium in DMSO into 1-salicyloyl-3-ethylhydantoin (**8**).

In the course of an investigation of the properties of benzyloxyamino acid esters of *N*-ethylsalicylamide,[1] we noted a ready decomposition of these substances under basic conditions and a formation of benzyl alcohol, along with one of a series of new, highly crystalline, neutral substances. Ring–chain tautomerism of an unusually rich kind was a possible complication for these species, and in this paper we wish to present evidence which establishes the structure of the simplest of these species and which determines the facility with which it equilibrates with its tautomers.

When *O*-benzyloxycarbonylglycyl-*N*-ethylsalicylamide[2] (**1**) is treated in acetonitrile solution with triethylamine, a red, tarry mixture of products is formed from which a highly crystalline substance, X, $C_{12}H_{12}N_2O_4$, is readily isolable. Careful saponification of this



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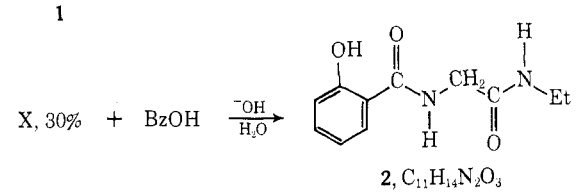

2, $C_{11}H_{14}N_2O_3$

substance results in a nearly quantitative conversion to salicyloylglycine ethylamide (**2**), an observation which establishes an amide insertion reaction of the

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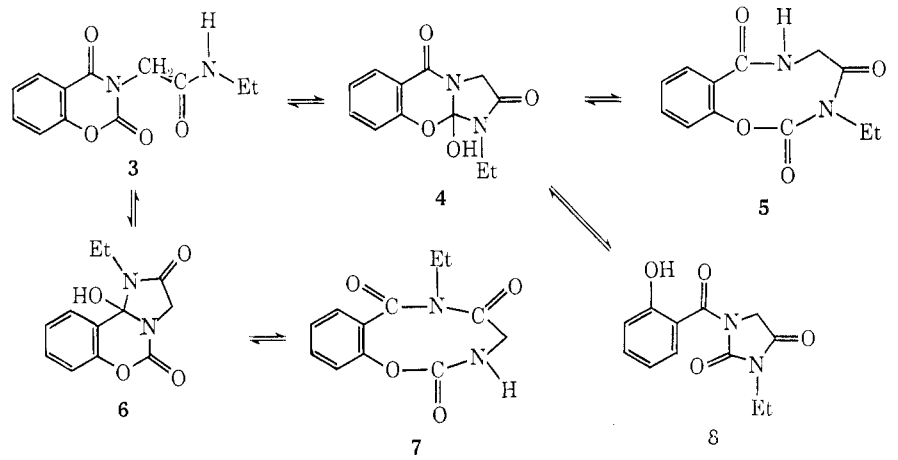
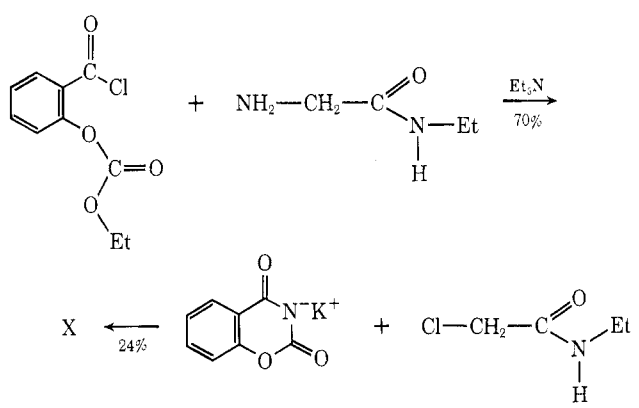
(1) D. S. Kemp and R. B. Woodward, *Tetrahedron*, **21**, 3019 (1965); D. S. Kemp, *ibid.*, **23**, 2001 (1967); D. S. Kemp, Ph.D. Thesis, Harvard University, 1964.

(2) D. S. Kemp, S. W. Wang, G. Busby III, and G. Hugel, *J. Amer. Chem. Soc.*, **92**, 1050 (1970).

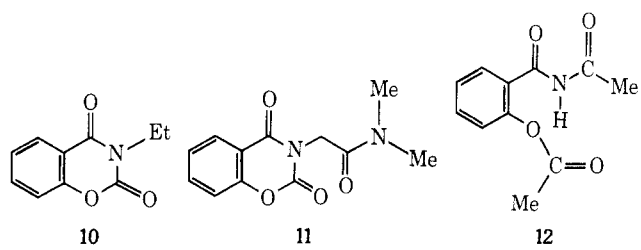


Brenner type[3] to have occurred between **1** and **2**, and which moreover establishes the likely existence of the glycine amide and salicyloyl moieties of **1** as elements of the structure of X. Even with this restriction there remained a problem of selecting one among six structures (**3**–**8**) for X, each of which might be supposed to be in equilibrium with the others *via* a series of internal carbonyl additions.[4,5] Provided these equilibrations could be established as occurring slowly, the observation that X is obtainable in two alternative ways as shown below is very strong support for assignment of structure **3** to X, but in the absence of such information these independent syntheses contribute nothing to



the resolution of the problem beyond further support for the prior conclusion that X contains salicyloyl and glycine amide moieties.

In organic solvents the infrared carbonyl absorption of X shows a characteristic two-band pattern (Figure 1 and Table I) which by comparison with models **10** and **11** appears to rule out structure **6**. The observation that **12**, which may be regarded as a rough



model for the macrocycle **7**, shows a carbonyl absorption pattern nearly identical with that of X indicates that, without further model information, infrared evidence is insufficient to exclude the remaining structures.

TABLE I

IR ABSORPTION OF X AND MODEL SUBSTANCES IN CH_2Cl_2

Substance	Carbonyl absorption, cm^{-1}
X	1705, 1765
10	1705, 1765
12	1698, 1766
Y	1705, 1765

Evidence supportive of the cyclol structure **6** was obtained when X was treated with triethyloxonium ion, followed by triethylamine. An ethylated substance, Y, is obtained whose infrared carbonyl absorption is that of X, yet is clearly demonstrated by its nmr spectrum to possess an ethoxy function. Of the tautomers **3**–**8**, only **6** meets the infrared data and possesses an OH function convertible to an ethoxyl group.

$$\underset{C_{12}H_{12}N_2O_4}{X} + Et_3O^+BF_4^- \longrightarrow \underset{C_{14}H_{16}N_2O_4}{Y}$$

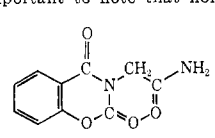
On the other hand, nmr data for X itself are only compatible with structure **3**. While initial observations of X, which for solubility reasons were conducted in trifluoroacetic acid, showed the *N*-ethylmethylene resonance as a quartet, other measurements carried out in deuterated DMSO, DMF, or pyridine showed a well-defined quintet for this resonance, a result which requires the ethylamide function to be secondary.

At this juncture the choice lay between assignation of **3** as the structure of the substance which carries with it the conclusion that the secondary amide carbonyl absorption for this substance falls at the anomalously high value of 1735 cm^{-1}, or the view that the molecule

(3) M. Brenner, *et al.*, *Helv. Chim. Acta*, **40**, 1497 (1957).

(4) For reviews of ring–chain tautomerism, see P. R. Jones, *Chem. Rev.*, **63**, 461 (1963); G. S. Hammond in M. R. Newman, "Steric Effects in Organic Chemistry," Wiley, New York, N. Y., 1966, p 460.

(5) Still more extravagant examples of ring–chain tatutomeric behavior are, in principle, possible in related systems; **9**, for example, is one among ten tautomers. It is important to note that none of the structures **3**–**8**



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are *a priori* excludable on grounds of stability. The presence of but a single saturated atom in **5** and **7** rules out internal nonbonded interaction as a destabilizing feature of these nine-ring species, while the observation of equilibria which favor cyclol isomers for not dissimilar systems[6] requires that **4** and **6** be considered as structural possibilities.

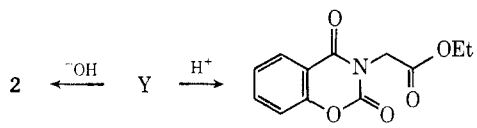
(6) R. G. Griot and A. J. Frey, *Tetrahedron*, **19**, 1661 (1963).

is a veritable Proteus, able to interconvert in a variety of media among the structures **3–8**, and that the nmr and ir observations taken in different media in fact correspond to different structures.

The observation that a sample of independently synthesized 3-salicyloyl-1-ethylhydantoin (**8**) is distinct from X and shows no tendency to equilibrate with it under mild conditions implies that ring–chain tautomeric shifts, at least in the series **3–4–8**, are not facile for these substances.

At the same time, the observation that the solid state infrared spectra (KBr) of X and **11** are identical in the carbonyl region, showing absorption maxima at 1645, 1700, and 1760 cm^{-1}, may be taken to support either the structural assignment of **3** with emphasis on the anomalous solution spectrum of this substance or the notion of limited but facile ring–chain interconvertability.

Further support for the assignment of **3** to X was available from the hydrolysis behavior of Y, which under basic conditions yields **2** and under acetic conditions, the ethyl ester, **13**, independently synthesized from ethyl chloroacetate and the sodium salt of *O,N*-carbonylsalicylamide. This latter observation is com-



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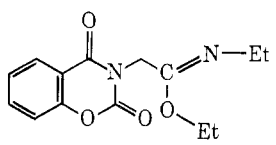
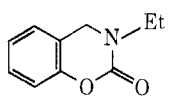
pletely consistent with assignment of the imino ether structure **14** to Y, but quite inconsistent with assignment of a structure such as the ethyl ether of the cyclol **6**. The anomalous infrared absorption of this imino



14 ≡ Y

ether, which lacks the characteristic absorption at *ca.* 1650 cm^{-1},[7] remains unexplained.

Conclusive evidence for the structural assignment of **3** to X is provided by the ultraviolet spectral data summarized in Table II. A crude model for the chromophore of the cyclol **6** is provided by the urethane **15**.[8]



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The observation of ultraviolet absorption identical in all qualitative features for the 1,3-benzoxazine-2,4-dione derivatives **10**, **11**, and **13**, as well as for X, a finding which holds in dichloromethane as well as in ethanol, firmly establishes **3** as the structure for X in both hydroxylic and nonhydroxylic solvents.[10] The

(7) *Cf.*, for example, H. Peter, M. Brugger, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **46**, 579 (1963).

(8) Synthesized by Raney nickel desulfurization of 3-ethyl-1,3-benzoxazine-4-thia-2,4-dione.[9]

(9) D. S. Kemp and R. B. Woodward, *Tetrahedron*, **21**, 3034 (1965).

(10) In the light of the amide absorption in CH_2Cl_2 at 1705 cm^{-1} which **3** exhibits, it is of interest to note that *N*-alkylamides in the vapor phase or in very dilute solutions are reported to lie in the range of 1720–1700 cm^{-1}.[11] Also pertinent is the absorption of phthalimidoglycylethylamide at 1780 (weak), 1720 (strong), and 1680 cm^{-1} (shoulder).

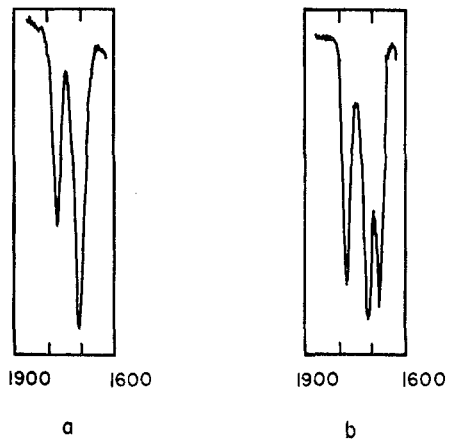


Figure 1.—Infrared carbonyl absorption (dichloromethane): a = X; b = **11**.

TABLE II
ULTRAVIOLET SPECTRAL DATA

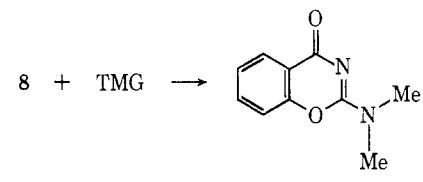
Substance	λ_{max}, mμ (EtOH)	ε
10	236	10,300
	238	9,980
	288	2,420
	295	2,030
13	236	11,200
	288	2,400
	297	2,120
14 ≡ Y	238	11,500
	288	2,400
	296	2,120
11	236	11,800
	287	2,500
	295	2,210
3 ≡ X	237	12,600
	288	2,600
	297	2,260
15	225	3,450
	267	904
	275	739
8	238	9,460
	306	4,460
12	sh 240	2,000

conversion of **1** to **3** is best regarded as strictly analogous to a simple Brenner rearrangement,[3] for which likely intermediates are *N*-benzyloxycarbonylglycyl-*N*-ethylsalicylamide and *N*-salicyloyl-*N*-ethoxycarbonylglycylethylamide.

A remaining question was whether the ring–chain tautomerism of **3** to **8** could be observed under any conditions and the availability of **3** to **8** made it possible to examine this point. When either of these substances was allowed to remain overnight in acetonitrile containing triethylamine, only starting materials and hydrolysis products were isolated. Substitution of the stronger base, tetramethylguanidine, resulted in the recovery of starting material and **2** from **3**, and of

(11) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Wiley, New York, N. Y., 1958, p 209.

3-ethylhydantoin and 2-dimethylamino-1,3-benzoxazin-4-one (**16**), identified by its formula and spectral features, from **8**. On the other hand, treatment of



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3 for 3 hr at 25° with sodium methylsulfinylmethide in DMSO resulted in conversion to **8**, isolable in *ca.* 30% yield along with 17% starting material; longer reaction times resulted in more extensive decomposition. Although other components were present in trace amounts, no attempt was made to identify them. While the presence of small amounts of **4**, **5**, **6**, and **7** cannot be excluded, it may be noted that the anion of **8** would be expected to be favored under the strongly basic reaction conditions. Clearly the conceptual mechanistic scheme which interconverts **3** with its ring–chain tautomers requires excessively severe conditions to realize it in practice.

Experimental Section

All melting points are corrected. Unless otherwise stated, magnesium sulfate was used as a drying agent. Infrared spectra were recorded with a Perkin-Elmer 237 spectrometer, ultraviolet spectra with Cary 11 and 14 spectrometers, and nmr spectra with a Varian A-60 spectrometer, using tetramethylsilane as an internal standard. Microanalyses were performed by Scandinavian Microanalytical Laboratory, Copenhagen, Denmark, and Galbraith Laboratories, Knoxville, Tenn. Unless otherwise stated, solvents and reagents were Spectro or Reagent Grade.

3-(*N*-Ethylacetamido)benzoxazine-2,4-dione (3). 1. From *O*-Benzyloxycarbonylglycyl-*N*-ethylsalicylamide (1).[12]—To a solution of 19 g (0.06 mol) of **1** in 100 ml of dry MeCN was added 4.5 g (0.05 mol) of triethylamine. After 24 hr at 25° the solution was taken to dryness *in vacuo* and the resulting dark red residue combined with 10 ml of CH_2Cl_2 and 10 ml of cyclohexane. The resulting solid was collected and washed with CH_2Cl to yield 4.4 g, 32%, mp 248.0–250.0°. Recrystallization from MeCN yielded a sample: mp 249.5–250.0°; nmr (CF_3CO_2H) δ 1.3 (t, 3, J = 7 Hz), 3.5 (quartet, 2, J = 7 Hz), 5.6 (s, 2), 7.9 (m, 5); nmr (pyridine) δ 1.0 (t, 3, J = 7 Hz), 3.3 (quintet, 2, J = 7 Hz), 4.9 (s, 2), 7.2–8.2 (m, 4), 8.5 (s, broad, 1). *Anal.* Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 57.96; H. 5.02; N, 11.10.

2. From 1,3-Benzoxazine-2,4-dione and *N*-Ethylchloroacetamide.[13]—To a stirred suspension of 8.15 g (50 mmol) of **17** and 1.40 g (58 mmol) of NaH in 100 ml of DMF was added 6.7 g (55 mmol) of *N*-ethylchloroacetamide. After 7 hr at 25° and 80° for 1 hr, the slurry was chilled and filtered, and the filtrate was concentrated *in vacuo*. The residue, 5 g, was recrystallized from methanol to yield 3.0 g of **3**, mp 248–250°, 24%, mmp 248.5–250°.

3. From Glycine Ethylamide and Ethoxycarbonylsalicyloyl Chloride.[14]—Benzyloxycarbonylglycine ethylamide was prepared from ZGlyOH and ethylamine, mp 100.7–101.2°. *Anal.* Calcd for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 60.86; H, 6.94; N, 11.89.

Hydrogenation of this substance followed by treatment with HCl yielded glycine ethylamide hydrochloride, mp 140.5–141.2°. *Anal.* Calcd for $C_4H_{11}N_2OCl$: C, 34.63; H, 8.00; N, 20.21; Cl, 25.58. Found: C, 34.48; H, 8.25; N, 19.21; Cl, 25.48.

To a stirred, ice-cooled solution of 0.3 g (2 mmol) of glycine ethylamide hydrochloride and 0.44 g (4 mmol) of triethylamine in 25 ml of CH_3CN was added dropwise 0.5 g (2 mmol) of ethoxycarbonylsalicyloyl chloride. The solution was stirred for 30 min at 25° and then was concentrated. The residue was dissolved in CH_2Cl_2, and the solution was extracted with two 10-ml portion of 1 *N* HCl, two 10-ml portions of 5% $NaHCO_3$, and 10 ml of water and then was dried, concentrated, and seeded to yield 0.37 g of solid, mp 249.0–.250.0°, 69%, mmp 250.0–251.0°.

3-(*N*,*N*-Dimethylacetamido)-1,3-benzoxazine-2,4-dione (11).—By the procedure outlined in 2 above, *N*,*N*-dimethylchloroacetamide was combined with the potassium salt of *O*,*N*-carbonylsalicylamide[15] in DMF. After 10 hr at 110°, the mixture was filtered, and the filtrate was evaporated *in vacuo*. The resulting oil was dissolved in CH_2Cl_2, and the solution was filtered to remove starting material. Evaporation, followed by several crystallizations from ethanol, yielded 20% of product, mp 162–163.5°, identical with a sample prepared from glycine dimethylamide and ethoxycarbonylsalicyloyl chloride. *Anal.* Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.01; H, 4.94; N, 11.19.

3-(Acetamido)-1,3-benzoxazine-2,4-dione.—By the procedure outlined in 2, chloroacetamide was combined with the potassium salt of *O*,*N*-carbonylsalicylamide in DMF. After 9 hr of heating, the mixture was cooled and filtered. The filtrate was concentrated *in vacuo* to an oil which was crystallized from ethanol to give 30% of product, 258.5–260° dec (lit.[14] 250° dec). Recrystallization raised the melting point to 264.5–266.5°. *Anal.* Calcd for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.30; H, 3.78; N, 12.61.

Reactions of 3-(*N*-Ethylacetamido)-1,3-benzoxazine-2,4-dione (3). 1. Alkaline Hydrolysis. Salicyloylglycine *N*-Ethylamide (2).—A solution of 48 mg of **3** in 3 ml of 1:1 acetone–water was subjected to the slow addition (3 hr) of 1.5 equiv of 0.1 *N* sodium hydroxide solution. The resulting solution was acidified to pH 1, stripped of acetone *in vacuo*, and extracted with ethyl acetate. Drying and evaporation yielded a residue which was recrystallized from ethyl acetate–cyclohexane to yield 30 mg of solid, mp 161–163°, identical in all respects with samples prepared by Brenner rearrangement of *O*-glycyl-*N*-ethylsalicylamide or by saponification of the product obtained from *O*-acetoxybenzoyl chloride and glycine *N*-ethylamide. Recrystallization yielded a sample: 165.0–165.8°; ir (KBr) 1680 (amide C=O), 1650 cm^{-1} (salicylamide C=O). *Anal.* Calcd for $C_{11}H_{14}N_2O_3$: C, 59.44; H, 6.35; N, 12.61. Found: C, 59.30; H, 6.55; N, 12.53.

2. Alkylation with Triethyloxonium Fluoroborate.—To a solution of 0.27 g (1.4 mmol) of triethyloxonium fluoroborate in 8 ml of dichloromethane was added 0.32 g (1.3 mmol) of **3**, and the resulting suspension was refluxed for 40 min at which point a clear solution was observed. The solution was extracted successively with 0.5 *N* sodium bicarbonate and water and then was dried and evaporated. The residue was extracted repeatedly with hot cyclohexane. Evaporation and crystallization from cyclohexane yielded 0.18-g plates (50%) of **14**: mp 105–106.5°; ir ($CHCl_3$) 1770, 1705 cm^{-1}; nmr ($CDCl_3$) δ 1.1 (t, 3, J = 7.5 Hz), 1.2 (t, 3, J = 7.5 Hz), 3.35 (quartet, 2, J = 7.5 Hz), 4.0 (quartet, 2, J = 7.5 Hz), 4.8 (s, 2), 7.2–8.2 (m, 4). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H 5.84; N, 10.10. Found: C, 61.04; H, 5.95; N 10.04.

When 85 mg of the above product was heated to boiling in 7 ml of ethanol and 0.5 ml of 0.1 *N* hydrochloric acid and then was cooled a yield of 68 mg (91%) of product precipitated, mp 126–127°. This substance was identical in all respects with 3-carbethoxymethyl-1 3-benzoxazine-2,4-dione (**3**), prepared by the alkylation of the potassium salt of *O*,*N*-carbonylsalicylamide with ethyl chloroacetate.[15]

When 48 mg of the above product was dissolved in a minimum volume of ethanol containing a few drops of 2 *N* sodium hydroxide, and the resulting solution was acidified with hydrochloric acid after 10 min at 25°, filtered, and concentrated, 34 mg (88%) of salicyloylglycine ethylamide (**2**) was obtained, identical in all respects with a sample obtained as described above.

3. Reaction with Bases in Aprotic Solvents.—A solution of sodium methylsulfinylmethide was prepared by dissolving 50 mg (2 mmol) of sodium hydride (washed free of oil with hexane) in 10 ml of dry DMSO. To this was added 250 mg (1 mmol) of **3**, and the resulting solution was stirred at 25° for 3 hr. The orange mixture was neutralized with 1.1 ml of 1 *N* hydrochloric acid, and the solvents were removed *in vacuo*. The residual oil

(12) D. S. Kemp, S. W. Wang, G. Busby, III, and G. Hugel, *J. Amer. Chem. Soc.*, **92**, 1050 (1970).

(13) W. Jacobs and W. Hiedelberger, *J. Biol. Chem.*, **21**, 145 (1915).

(14) E. Fisher and R. Freundenberg, *Justus Liebigs Ann. Chem.*, **372**, 36 (1910).

(15) A. Einhorn and C. Mettler, *Chem. Ber.*, **35**, 3650 (1902).

was partitioned between water and ethyl acetate, and the organic phase was dried and concentrated. Three crops of starting material totaling 40 mg (17%) were recovered. The aqueous phase, upon evaporation yielded 4 mg (3.4%) of 3-ethylhydantoin. Preparative tlc of the residual organic phase on silica gel using ethyl acetate–chloroform, 1:1 as eluent yielded a main fraction of 66 mg (27%) of 1-salicyloyl-3-ethylhydantoin (**8**), identified by infrared spectrum and melting point which was undepressed upon admixture of an authentic sample.

3-Ethyl-1,3-benzoxazin-2-one (**15**).—Roughly 10 g of Raney nickel was washed with water and dioxane and then added to a solution of 2.0 g of 3-ethyl-4-thio-1,3-benzoxazine-2,4-dione in 25 ml of dioxane. The slurry was stirred at room temperature for 30 min whereupon an additional 5 g of washed Raney nickel was added. After a further 45 min, the liquid was decanted, and the catalyst was washed with three 20-ml portions of dioxane. Concentration yielded an oil which was applied to an alumina column (40 g) and eluted with benzene–ethyl acetate. The product was recrystallized from cyclohexane: yield 30%; mp 57.0–58.0°; ir ($CHCl_3$) 1710 cm^{-1} (carbonate C=O); nmr ($CDCl_3$) δ 1.3 (t, 3, J = 7 Hz), 3.5 (quartet, Z, J = 7 Hz), 4.5 (s, 2), 7.1 (m, 4). *Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.96; H, 6.37; N, 7.87.

1-Salicyloyl-3-ethylhydantoin (**8**). **A. O-Benzyloxybenzoyl Chloride.**[16]—A solution of 7.5 g of *O*-benzyloxybenzoic acid in 10 ml of thionyl chloride was allowed to stand for 1 hr and then was heated intermittantly for 30 min until gas evolution ceased. The excess thionyl chloride was removed *in vacuo* and the residual oil was flash distilled in a short-path still equipped with a pressure-equalizing dropping funnel. The pot temperature was maintained at 200–210° and the still head was heated to 160–170° with a heating tape. The substance boils in the range 160–165° (0.1 mm), yield 5.8 g, 68%. If carefully freed of excess oxalyl chloride by evacuation, product prepared by reaction of *O*-benzyloxybenzoic acid with oxalyl chloride in benzene may be used without distillation.

2. 1-(O-Benzyloxybenzoyl)-3-ethylhydantoin (**18**).—*O*-Benzyloxybenzoyl chloride (4.5 g, 18 mmol) was added in small portions, with stirring, to a solution prepared by adding 2.1 g (17 mmol) of 3-ethylhydantoin[17] to 10 ml of dry DMF containing 0.44 g (18 mmol) of washed sodium hydride. After 30 min the solvent was removed *in vacuo* and the residue was triturated with 250 ml of ether. A solid was collected, washed with water, and recrystallized from ethanol to yield 1.4 g (25%) of product, mp 139.5–140.0°. An additional 0.6 g of product could be recovered from the ether filtrate (total yield, 35%). Recrystallization from ethanol raised the melting point to 141.5–142.5°. *Anal.* Calcd for $C_{19}H_{18}N_2O_4$: C, 67.45; H, 5.36; N, 8.28. Found: C, 67.53; H, 5.20; N, 8.14.

3. 1-Salicyloyl-3-ethylhydantoin (**8**).—A solution of 1.9 g (5.7 mmol) of **18** in 15 ml of ethyl acetate and 20 ml of dioxane was treated with 0.2 g of 5% palladium on carbon, purged with nitrogen, and hydrogenated at 1 atm, 25° for 8 hr. The resulting suspension was filtered, the solvent was stripped, and the solid residue was recrystallized from ethyl acetate–cyclohexane to yield 1.3 g (90%) of crude product. Recrystallization yielded material of mp 113.5–115°: ir (CH_2Cl_2) 3350, 1800, 1745, 1650 cm^{-1}; nmr ($CDCl_3$) δ 1.25 (t, 3, J = 7.5 Hz), 3.6 (quartet, 2, J = 7.5 Hz), 4.5 (s, 2), 6.7–7.2 (m, 4), 9.5 (s, 1). *Anal.* Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.28. Found: C, 58.30; H, 4.93; N, 11.34.

Reaction of 1-Salicyloyl-3-ethylhydantoin with Tetramethylguanidine. 2-Dimethylamino-1,3-benzoxazin-4-one (**16**).—A solution of 0.25 g (1 mmol) of **8** and 0.13 g of tetramethylguanidine in 10 ml of acetonitrile distilled from P_2O_5 was stirred at room temperature for 24 hr in a flask equipped with drying tube. The mixture was then neutralized with 1.1 ml of 1 *N* hydrochloric acid and evaporated to dryness. Trituration in ethyl acetate followed by filtration resulted in the recovery of 0.8 g of tetramethylguanidine hydrochloride. By repeated evaporation and trituration with ether, a total of 0.07 g of crude **16** was obtained. Recrystallization yielded 31 mg (16%): mp 152–153°; ir (CH_2Cl_2) 1675 cm^{-1} (C=O). *Anal.* Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.01; H, 5.44; N, 14.58.

Registry No.—**1**, 26595-68-6; **2**, 4611-36-3; **3**, 26595-70-0; **8**, 26595-71-1; **11**, 26595-73-3; **14**, 26595-72-2; **15**, 26595-74-4; **16**, 776-70-5; **18**, 26595-76-6; benzoylcarbonylglycine ethylamide, 21855-73-2; glycine ethylamide hydrochloride, 26595-78-8; 3-(acetamido)-1,3-benzoxazine-2,4-dione, 26600-29-3.

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