Anal. Calcd. for $C_7H_8N_4OS$: C, 42.84; H, 4.11. Found: C, 42.87; H, 4.25.

3(5)-Pyrazolecarboxylic Acid Hydrazide and Carbon Disulfide (a).—A mixture of 3.1 g. (0.025 mole) of 3(5)-pyrazolecarboxylic acid hydrazide,[16] 1.3 g. of potassium hydroxide and 5 ml. of carbon disulfide in 50 ml. of ethyl alcohol was stirred together at room temperature for 30 minutes. About 50 ml. of dry ether was added and the product separated in almost quantitative yield. Potassium 3-(3(5)-pyrazolecarbonyl)-dithiocarbazate (VII) melted with decomposition at about 210°, resolidified and melted again with dec. at 255–260°; λ_{max} 303 mμ, log ε 4.01 (methanol).

Anal. Calcd. for $C_5H_5KN_4OS_2$: C, 24.98; H, 2.10; N, 23.31; S, 26.68. Found: C, 25.37; H, 2.34; N, 23.60; S, 26.85.

A sample of potassium 3-(3(5)-pyrazolecarbonyl)-dithiocarbazate was heated at 230° for 15 minutes. The product was dissolved in water and acidified with dilute hydrochloric acid. The solid that formed was collected and recrystallized from water. It was shown by infrared data to be identical with compound VIII (see below).

(b).—A mixture of 6.3 g. (0.05 mole) of 3(5)-pyrazolecarboxylic acid hydrazide,[16] 2.8 g. (0.05 mole) of potassium hydroxide, 5 ml. of carbon disulfide and 200 ml. of ethyl alcohol was heated under reflux for three days. After removal of the alcohol the residue was dissolved in 100 ml. of water and acidified with dilute hydrochloric acid. The solid that separated was collected, washed well with water and air-dried. It melted between 200 and 205°. The product[17] was recrystallized from methanol–water mixture and 5.3 g. (63% yield) of 2-(3(5)-pyrazolyl)-Δ^2-1,3,4-oxadiazoline-5-thione (VIII) was obtained. A sample was recrystallized from methanol and obtained as a white solid, m.p. 220° dec.; λ_{max} 241 mμ, log ε 3.89; λ_{max} 286 mμ, log ε 4.24 (methanol); pK'_a 5.4 (66% dimethylformamide).

(16) L. Knorr, *Ber.*, **37**, 3520 (1904).

(17) The first lot of this material was treated with Raney nickel and a small yield of compound XI was isolated, indicating that the product of this lot was a mixture of compounds VIII and X. Subsequent preparations did not appear to contain any of compound X.

Anal. Calcd. for $C_5H_4N_4OS$: C, 35.71; H, 2.40; N, 33.32. Found: C, 35.86; H, 2.60; N, 33.05.

A mixture of 2 g. of 2-(3(5)-pyrazolyl)-Δ^2-1,3,4-oxadiazoline-5-thione, 50 ml. of 95% ethyl alcohol and 5 g. of moist Raney nickel was heated under reflux for three hours. After removal of the nickel by filtration the filtrate was evaporated to dryness. The residue was recrystallized from hot water, and on cooling 200 mg. of 2-(3(5)-pyrazolyl)-1,3,4-oxadiazole (IX) was deposited. It melted at 200–202°. A sample was obtained by sublimation, m.p. 204–205°; λ_{max} 236 mμ, log ε 4.06 (methanol).

Anal. Calcd. for $C_5H_4N_4O$: C, 44.12; H, 2.96; N, 41.17. Found: C, 44.13; H, 3.11; N, 41.20.

7-Mercaptopyrazolo[1,5-*d*]*as*-triazin-4(5*H*)-one (X).—A sample of 2-(3(5)-pyrazolyl)-Δ^2-1,3,4-oxadiazoline-5-thione was heated at 200° and 0.5 mm. of mercury pressure. The product that was obtained as the sublimate was 7-mercaptopyrazolo[1,5-*d*]*as*-triazin-4-(5*H*)-one, m.p. 201–202°; λ_{max} 234 mμ, log ε 3.81; λ_{max} 262 mμ, log ε 4.11; λ_{max} 297 mμ, log ε 4.09 (methanol); pK'_a 4.1 (66% dimethylformamide).

Anal. Calcd. for $C_5H_4N_4OS$: C, 35.71; H, 2.40; S, 19.07. Found: C, 35.37; H, 2.52; S, 18.64.

A mixture of 1 g. of 7-mercaptopyrazolo[1,5-*d*]*as*-triazin-4(5*H*)-one, 50 ml. of 95% ethyl alcohol and 5 g. of moist Raney nickel was heated under reflux for six hours. After removal of the nickel by filtration, the filtrate was evaporated to dryness. The residue was dissolved in a small amount of 1 *N* sodium hydroxide and then acidified with acetic acid. The solid that separated was recrystallized from water and pyrazolo[1,5-*d*]*as*-triazin-4(5*H*)-one (XI) was obtained as needles, m.p. 265–267°; λ_{max} 264 mμ, log ε 3.86 (methanol). The melting point was not depressed when mixed with pyrazolo[1,5-*d*]*as*-triazin-4(5*H*)-one[10] prepared from 3(5)-pyrazolecarboxylic acid hydrazide and triethyl orthoformate.

Anal. Calcd. for $C_5H_4N_4O$: C, 44.12; H, 2.96; N, 41.17. Found: C, 43.95; H, 3.35; N, 41.17.

INDIANAPOLIS 6, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Reaction of Phthaloylglycyl Chloride with 2-Methyl-2-thiazoline[1]

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As part of a program directed toward the synthesis of compounds structurally related to the penicillins, the reaction of phthaloylglycyl chloride (I) with 2-methyl-2-thiazoline (II) in the presence of triethylamine has been studied. Rather than yielding a β-lactam-thiazolidine structure, expected by analogy to the 2-phenyl-2-thiazoline case, the reaction leads to 2-methylene-3-phthaloylglycylthiazolidine (III) at low temperature and in the presence of one equivalent of base, and to 2-methyl-3-phthaloylglycyl-4-thiazoline (V) at higher temperatures and in the presence of excess base. The structures of compounds III and V were established by hydrogenation to 2-methyl-3-phthaloylglycylthiazolidine (VI). A mechanism for the reaction is proposed. Analogous products were obtained using phthaloyl-β-alanyl chloride (Ia) as the acylating agent.

The reaction of diacyl glycyl chlorides with 2-phenyl-2-thiazolines in the presence of triethylamine, yielding fused β-lactam-thiazolidine ring systems, has been a promising approach toward the synthesis of penicillin-type compounds.[3] In an investigation of the scope of this synthesis, we have studied the action of phthaloylglycyl chloride (I) and phthaloyl-β-alanyl chloride (Ia) on 2-methyl-2-thiazoline (II).

It was found that, depending on reaction conditions, either of two distinct types of products was formed. In the presence of one equivalent of triethylamine, I and II formed a "low temperature adduct" III, which precipitated together with triethylammonium chloride. The products were best separated by an aqueous wash, which converted III into a crystalline "hydrated adduct" IV with the addition of one equivalent of water. At 60°, and in the presence of excess triethylamine, a "high temperature adduct" V was obtained, which is isomeric with III, but which did not take up water on washing. Under conditions lying between these two extremes, products were formed which, after washing with water, analyzed for mixtures of compounds IV and V.

None of the products obtained possesses infrared absorption indicative of a β-lactam structure.

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(2) Abstracted from parts of the Ph.D. Dissertations of J. J. Ryan, M.I.T., June 1949, and C. W. Beck, M.I.T., January 1955.

(3) J. C. Sheehan and G. D. Laubach, THIS JOURNAL, **73**, 4376 (1951).

Qualitative tests showed that free carboxyl groups were absent (insolubility in aqueous sodium hydroxide), and left the presence of basic centers in doubt (solubility in 3 *N* hydrochloric acid only with decomposition and concurrent liberation of sulfhydryl groups). The relative instability of compounds III and IV is further underlined by decomposition on storage at room temperature for as short a period of time as one week. The decomposition products, as well as the hydrolysis products, were amorphous and resisted efforts at identification.

This evidence may be reconciled either with an intact thiazoline ring structure, or with ring scission leading to N,S-diacylthioethanolamines. The infrared spectra of all three "adducts" were similar, and were strikingly reminiscent of the spectra of substituted thiazolines. A Kuhn–Roth C-methyl determination[4] on the "high temperature adduct" V yielded 0.83 equivalent of acetic acid, very close to the value of 0.80 equivalent obtained from 2-methyl-2-thiazoline under identical conditions.

If both the high and low temperature "adducts" indeed are substituted N-phthaloylglycylthiazolines, hydrogenation should lead, in either case, to 2-methyl-3-phthaloylglycylthiazolidine (VI). The latter compound was prepared, for comparison, by direct acylation of 2-methylthiazolidine (VII) with phthaloylglycyl chloride (I) in the presence of triethylamine.

Hydrogenation of the "low temperature adduct" III over 30% palladium-on-carbon catalyst[5] was complete in four hours, yielding, after recrystallization, 60% of a product which was shown to be identical with VI by melting point, mixed melting point, infrared spectra and double analyses. The "high temperature adduct" V proved much more resistant to hydrogenation, but after several days, and with a threefold excess of catalyst (on a weight-to-weight basis), it absorbed 0.96 equivalent of hydrogen and yielded, after recrystallization, 46% of VI.

Thus both "adducts" differ from VI only by containing one double bond each. Positions available for double bond formation are limited to either (a) C_4–C_5, or (b) C_2-methylcarbon. Spectrographic evidence based on olefinic double bond absorption in the infrared cannot distinguish between these two cases; furthermore, in the compounds under consideration, the respective region (6.0–6.3 μ; 1670–1590 cm.$^{-1}$) is obscured by the absorption of the benzene ring of the phthaloyl group. However, exocyclic methylene groups show a very characteristic band at 11.43 μ (875 cm.$^{-1}$), due to C–H rocking.[6] A band in this region is present in both the "low temperature adduct" III and the "hydrated adduct" IV, but is missing in the "high temperature adduct" V, thus favoring the assignment of the 2-methylene-3-phthaloylglycylthiazolidine structure for III, and of the 2-methyl-3-phthaloylglycyl-4-thiazoline structure for V.

The formation of the two "adducts" under their respective reaction conditions can be rationalized convincingly. Figure 1 illustrates a possible mechanism leading to the established structures, as well as the reactions used in their identification. 2-Methyl-2-thiazoline (II) may be considered to be in prototropic equilibrium with the isomeric 2-methyl-3-thiazoline (imine) and 2-methyl-4-thiazoline (enamine) forms at least under the reaction conditions. Similar 1,3-proton shifts are known to be favored by excess base and elevated temperatures.[7] Thus either the 3- or the 4-thiazoline tautomer will be the reacting species at 60° and in the presence of excess triethylamine. Either of these lead to the 2-methyl-3-phthaloylglycyl-4-thiazoline structure established for the "high temperature adduct" V. Reaction at low temperatures and without excess base, on the other hand, leads to 2-methylene-3-phthaloylglycylthiazolidine, *i.e.*, the "low temperature adduct" III. An analogy for this type of prototropy is afforded by the Bergmann rearrangement[8] of oxazolones, where the imine → enamine → isomeric imine shift is catalyzed by pyridine. This reaction has been investigated previously in this Laboratory.[9]

The remaining problem concerns the nature of the water molecule in the "hydrated adduct" IV. As mentioned previously, the addition of water produces no major changes in the infrared spectrum. The characteristic band at 11.43 μ (875 cm.$^{-1}$), assigned to the exocyclic double bond in III, does not disappear. This position should be the preferred point of attack in any reaction leading to ring cleavage. It therefore appears that the water is only physically bound to the adduct, *i.e.*, that compound IV is a simple hydrate. In corroboration of this view, it was found that the "hydrated adduct" IV could be dehydrated by drying over phosphorus pentoxide at room temperature and low pressure. The dehydrated material, which melted lower than the hydrate, was not crystalline.

The reaction of phthaloyl-β-alanyl chloride (Ia) with 2-methyl-2-thiazoline (II) was also studied. At 60°, in the presence of excess triethylamine, there was obtained a "high temperature adduct" (Va), which was found to be a homolog of V. The basic skeleton was established by hydrogenation, in which Va took up one mole of hydrogen and gave an 80% yield of 2-methyl-3-phthaloyl-β-alanylthiazolidine (VIa). The latter was synthesized independently by direct acylation of 2-methylthiazolidine (VII) with phthaloyl-β-alanyl chloride (Ia). Oxidation of VIa with potassium permanganate in 80% acetic acid gave 2-methyl-3-phthaloyl-β-alanylthiazolidine sulfone (VIIIa), a reaction characteristic of N-acylthiazolidines.[10] The double bond in Va is assigned to the position C_4–C_5, rather than C_2-methylcarbon, by analogy with the structure of V, and by a Kuhn–Roth C-methyl determination[4] which gave 0.92 equivalent of acetic acid.

(4) R. Kuhn and H. Roth, *Ber.*, **66**, 1274 (1933).

(5) N. D. Zelinsky and M. B. Turowa-Pollak, *ibid.*, **58**, 1295 (1925).

(6) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons ,Inc., New York, N. Y., 1954, p. 44.

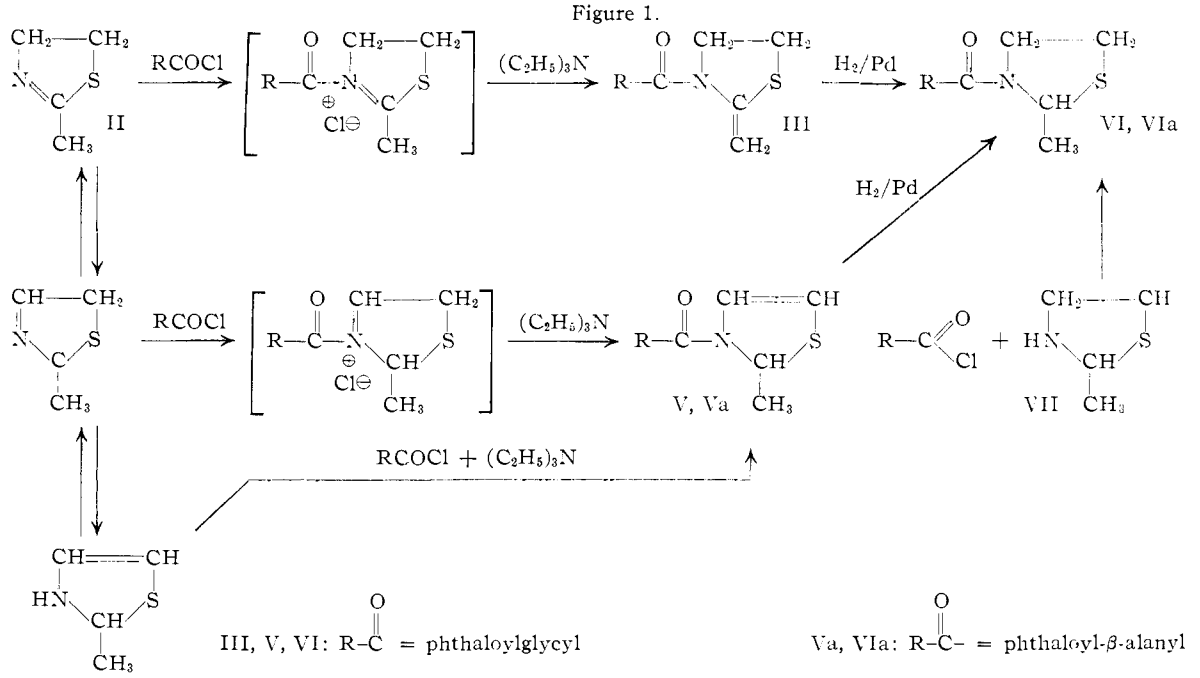
(7) W. Hückel, "Theoretische Grundlagen der Organischen Chemie," 1. Band, Akademische Verlagsgesellschaft, Leipzig, 1949, pp. 259 ff., 244, 526 ff.

(8) M. Bergmann and F. Stern, *Ann.*, **448**, 20 (1926).

(9) J. C. Sheehan and W. E. Duggins, THIS JOURNAL, **72**, 2475 (1950).

(10) H. T. Clarke, J. R. Johnson and R. Robinson, editors, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J. 1949, p. 929.

Figure 1.



Experimental[11]

The Reaction between Phthaloylglycyl Chloride and 2-Methyl-2-thiazoline. A. "Low Temperature Adduct" III.—A solution of 5.60 g. (0.0250 mole) of phthaloylglycyl chloride in anhydrous benzene was added dropwise to a stirred solution of 3.79 g. (0.0375 mole) of 2-methyl-2-thiazoline[12] and 2.53 g. (3.47 ml., 0.0250 mole) of triethylamine in anhydrous benzene at room temperature. The addition required 30 minutes. After stirring for an additional 30 minutes, the thick white precipitate was removed by filtration, washed with pentane, and dried at room temperature. The crude product weighed 9.4 g. or 88% of the combined theoretical weight of triethylammonium chloride and adduct.

Stirring the crude product with 200 ml. of water at 35° for 15 minutes, removing the insoluble material by filtration and drying under reduced pressure yielded 6.3 g. (82%) of "low temperature adduct." After one recrystallization from boiling acetone, the compound melted at 183.5–185° with partial decomposition, slight discoloration beginning at about 170°. Further recrystallizations from boiling acetone lowered the melting point of the material, which then no longer appeared crystalline. Recrystallizing a fresh portion by pouring boiling acetone over it, filtering rapidly, and cooling the filtrate in ice raised the melting point to 186–188° dec.

Anal. Calcd. for $C_{14}H_{12}N_2O_3S \cdot H_2O$: C, 54.89; H, 4.61; N, 9.15. Found: C, 54.63; H, 5.40; N, 9.21.

The same product was obtained by carrying out the addition at 0°.

B. "High Temperature Adduct" V.—To a solution of 2.02 g. (0.02 mole) of 2-methyl-2-thiazoline and 10.1 g. (0.10 mole) of triethylamine in 30 ml. of anhydrous benzene, a solution of 4.48 g. (0.02 mole) of phthaloylglycyl chloride in 50 ml. of anhydrous benzene was added dropwise while stirring rapidly and maintaining the temperature of the reaction mixture at 60°. The addition required 20 minutes. After stirring at room temperature for an additional 3 hours, the solid was removed by filtration, washed with dry benzene, and dried in a vacuum desiccator, yielding 6.3 g. (74%) of a light yellow material. After stirring this crude product in water at room temperature for 15 minutes, there remained 3.5 g. (61%) of a cream-colored solid, which melted at 197–199° dec. after three recrystallizations from boiling acetone.

Anal. Calcd. for $C_{15}H_{12}N_2O_3S$: C, 58.34; H, 4.20; N, 9.72. Found: C, 58.57; H, 4.34; N, 9.82.

Repetition of the run at 60°, but using only one equivalent of triethylamine, yielded, after washing with water and recrystallization from ethanol, 54% of a solid melting at 196–198° dec., which gave an analysis (found: C, 57.45; H, 4.36; N, 9.00) indicating a mixture of "low temperature adduct" III and "high temperature adduct" V.

2-Aminoethanethiol Hydrochloride.—To 75 ml. of 6 *N* hydrochloric acid was added 14.35 g. of freshly distilled 2-methyl-2-thiazoline[12] and the solution was refluxed for 21 hours under nitrogen. The colorless solution was concentrated at 70° (15 mm.) then flushed with 50-ml. portions of absolute ethanol, absolute ethanol–benzene and benzene. The resulting crystals were dried at 0.1 mm. to yield 15.79 g. (98%), m.p. 68–69°. Recrystallization from absolute ethanol–ether raised the melting point to 69.5–70.5° (reported[13] m.p., 70.2–70.7°).

2-Methylthiazolidine (VII).[14]—To a solution of 19.3 g. (0.142 mole) of sodium acetate trihydrate in 75 ml. of water, swept with a nitrogen stream, was added 15.8 g. (0.139 mole) of thioethanolamine hydrochloride. To this solution at 0–5° was added an ice-cold solution of 6.3 g. (0.142 mole) of acetaldehyde in 25 ml. of water with stirring over a period of 15 minutes. The solution was stored under nitrogen overnight at 5°; then 15 g. of sodium carbonate was added, and the mixture extracted with three 100-ml. portions of ether. The combined ethereal extracts were dried over calcium sulfate and concentrated at 35 mm. pressure. Distillation of the residue (11.1 g.) at atmospheric pressure yielded 9.4 g. (66%) of colorless liquid, b.p. 155–165°, $n^{25}D$ 1.5236–1.5255. Redistillation at reduced pressure under nitrogen afforded 6.9 g. of VII, b.p. 76–77° (36 mm.), $n^{25}D$ 1.5248–1.5255.

Anal. Calcd. for C_4H_9NS: C, 46.56; H, 8.79; N, 13.58. Found: C, 46.82; H, 8.93; N, 13.67.

2-Methyl-3-phthaloylglycylthiazolidine (VI).—To 1.03 g. (0.01 mole) of 2-methylthiazolidine and 1.01 g. (0.01 mole) of triethylamine in 10 ml. of dry methylene chloride, a solution of 2.24 g. (0.01 mole) of phthaloylglycyl chloride in 40 ml. of dry methylene chloride was added over a period of 90 minutes with stirring and cooling. The solvent was evaporated under reduced pressure and the residue recrystallized from boiling ethanol, yielding 2.0 g. (69%) of VI, m.p. 199–

(11) All melting points are corrected. We are indebted to Dr. S. M. Nagy and his associates for the microanalytical data.

(12) H. Wenker, THIS JOURNAL, **57**, 1079 (1935).

(13) E. J. Mills, Jr., and M. T. Bogert, *ibid.*, **62**, 1173 (1940).

(14) 2-Methylthiazolidine has been reported (H. Bestion, *Ann.*, **566**, 241 (1950)) to have b.p. 62–65° at an unstated pressure. The compound was prepared from ethylene imine, acetaldehyde and hydrogen sulfide.

200°. A second crop (m.p. 196–199°) of 0.4 g. was obtained by concentration of the filtrate, bringing the total yield to 83%.

Anal. Calcd. for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65. Found: C, 57.61; H, 5.01; N, 9.55.

Hydrogenation of the "Low Temperature Adduct" III.—A suspension of 3.75 g. of 30% palladium-on-charcoal catalyst[5] in 100 ml. of dry, purified dioxane was prereduced at room temperature and atmospheric pressure. The catalyst was separated by filtration, and the filtrate used to dissolve 1.48 g. of crude "low temperature adduct" containing theoretically 0.48 g. of triethylammonium chloride. Upon filtration, there remained 0.50 g. (104%) of insoluble triethylammonium chloride, m.p. 250–255°.

The prereduced catalyst was added to the dioxane solution, and the mixture was hydrogenated at room temperature and atmospheric pressure. At the end of 4 hours, 0.99 equivalent had been absorbed, and the reaction ceased. The catalyst was removed by filtration, washed with dioxane, and the combined filtrates were concentrated under reduced pressure. The remaining yellow oil crystallized on storage overnight in a refrigerator, yielding, after recrystallization from ethanol, 0.60 g. (60%) crystalline product, m.p. 197–199°. The mixed m.p. of the product with 2-methyl-3-phthaloylglycylthiazolidine (VI) was 196–199° (undepressed). The infrared spectra of the product and of compound VI were identical.

Anal. Calcd. for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65. Found: C, 57.90; H, 5.20; N, 9.41.

Hydrogenation of the "High Temperature Adduct" V.—A suspension of 3.75 g. of 30% palladium-on-charcoal catalyst[5] in 100 ml. of dry, purified dioxane was prereduced at room temperature and atmospheric pressure. Freshly prepared "high temperature adduct" V (0.65 g., 0.00226 mole) was added, and hydrogenation resumed. Addition of a second 3.75-g. portion of catalyst was necessary at the end of 24 hours; hydrogenation then proceeded smoothly, though slowly, until 0.96 equivalent had been taken up at the end of 4 days. The catalyst was removed by filtration and washed with dioxane. The combined filtrates were evaporated. The remaining oil solidified after storage in a refrigerator for 2 days. Recrystallization from ethanol yielded 0.3 g. (46%) of colorless material, m.p. 190–194°. A second recrystallization raised the melting point to 197–200°. A mixed m.p. with 2-methyl-3-phthaloylglycylthiazolidine (VI) was 197–199° (undepressed). The infrared spectra of this product and of authentic compound VI were identical.

Anal. Calcd. for $C_{14}H_{14}N_2O_3S$: C, 57.92; H, 4.86; N, 9.65. Found: C, 57.53; H, 5.10; N, 9.58.

Dehydration of the "Hydrated Adduct" IV.—A freshly recrystallized sample of 0.0415 g. (0.000135 mole) of "hydrated adduct" IV, previously dried at 70 mm. pressure, was dried at 0.05 mm. pressure and room temperature to constant weight. At the end of 5 days, the sample had lost 0.0023 g. (94% of theory for one mole of water), and melted gradually at 165–175°, after sintering at 160°. The material was not crystalline.

The Reaction between Phthaloyl-β-alanyl Chloride and 2-Methyl-2-thiazoline. "High Temperature Adduct" Va.—To a solution of 8.08 g. (0.08 mole) of 2-methyl-2-thiazoline and 40.5 g. (0.40 mole) of triethylamine in 120 ml. of anhydrous benzene in a 60° oil-bath was added a solution of 19.0 g. (0.08 mole) of phthaloyl-β-alanyl chloride (Ia) in 200 ml. of anhydrous benzene with rapid stirring over a period of 40 minutes. Stirring was continued for one hour at 60°, then overnight at room temperature. The colorless solid was removed by filtration, washed twice with anhydrous benzene and dried under reduced pressure to yield 20.5 g. After washing this crude product with six 100-ml. portions of water, filtration and drying under reduced pressure at room temperature afforded 10.1 g. (42%) of a solid which melted at 117–123° dec. Two rapid recrystallizations from boiling acetone gave colorless needles, m.p. 148–151° dec. Concentration of the original benzene mother liquors and recrystallization from acetone yielded an additional 2.34 g. (10%) of crude Va, m.p. 127–136° dec.

Anal. Calcd. for $C_{15}H_{14}N_2O_3S$: C, 59.58; H, 4.67; N, 9.27. Found: C, 59.61; H, 4.70; N, 9.44.

2-Methyl-3-phthaloyl-β-alanylthiazolidine (VIa).—To a solution of 0.80 g. (0.0078 mole) of 2-methylthiazolidine (VII) in 10 ml. of dry methylene chloride at −25° was added rapidly and with stirring a solution of 1.86 g. (0.0078 mole) of phthaloyl-β-alanyl chloride (Ia) in 40 ml. of dry methylene chloride, followed by the dropwise addition of a solution of 0.79 g. (0.0078 mole) of triethylamine in 25 ml. of methylene chloride over a period of 35 minutes. The cooling bath was removed, and the mixture stirred overnight. Concentration under reduced pressure and recrystallization of the residue from boiling ethanol gave 1.96 g. (82%), m.p. 132–134°. Two further recrystallizations from ethanol afforded colorless rosettes of needles, m.p. 138–141°.

Anal. Calcd. for $C_{15}H_{16}N_2O_3S$: C, 59.19; H, 5.30; N, 9.21. Found: C, 59.08; H, 5.44; N, 8.93.

Hydrogenation of the "High Temperature Adduct" Va.—A suspension of 1.75 g. of 30% palladium-on-charcoal catalyst[5] in 30 ml. of dry purified dioxane was prereduced at room temperature and atmospheric pressure for three days. The "high temperature adduct" Va (0.50 g., 0.00165 mole) was added and the hydrogenation resumed. At the end of 5 hours, 40.9 ml. (1.02 equivalents) of hydrogen had been absorbed. The catalyst was removed by filtration and the filtrate concentrated to a colorless, micro-crystalline solid, 0.40 g. (80%), m.p. 131–134°. Recrystallization from hot ethanol–water gave an analytical sample, m.p. 137.5–140°. A mixed melting point with authentic 2-methyl-3-phthaloyl-β-alanylthiazolidine (VIa) was 137.5–140.5°. The infrared spectra of this product and of compound VIa were identical.

Anal. Calcd. for $C_{15}H_{16}N_2O_3S$: C, 59.19; H, 5.30; S, 10.53. Found: C, 59.49; H, 5.48; S, 10.49.

2-Methyl-3-phthaloyl-β-alanylthiazolidine Sulfone (VIIIa).—To a solution of 0.40 g. (0.0013 mole) of VIa was added a solution of 1.43 g. (0.0091 mole) of potassium permanganate in 18 ml. of water. The solution was held at room temperature for 20 minutes, decolorized with 30% hydrogen peroxide, and then diluted with 200 ml. of water. After several days at 5°, 0.22 (50%) of colorless needles, m.p. 201–203° dec. was collected. Two recrystallizations from boiling absolute ethanol–acetone raised the melting point to 204–205° dec.

Anal. Calcd. for $C_{15}H_{16}N_2O_5S$: C, 53.56; H, 4.80; N, 8.33. Found: C, 53.66; H, 4.83; N, 8.38.

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