collected and recrystallized from methanolic acetonitrile and from acetonitrile to a constant melting point of 220–221° dec., to furnish 11 g. or 43% of isomer A. There was no loss in weight after drying at 65° at 0.1 mm.

Anal. Calcd. for $C_{14}H_{18}N_4O$: C, 65.09; H, 7.02; N, 21.69. Found: C, 65.15; H, 7.06; N, 21.75.

The acetonitrile liquor from which crude isomer A was obtained was concentrated to 40 ml. and chilled at −20° to furnish a buff solid. The solid was collected and recrystallized twice from acetonitrile to furnish 10.5 g. or 41% of white crystalline isomer B, m.p. 200–203° dec. There was no loss of weight after drying at 65° at 0.1 mm.

Anal. Calcd. for $C_{14}H_{18}N_4O$: C, 65.09; H, 7.02; N, 21.69. Found: C, 65.11; H, 6.82; N, 21.70.

Solutions of either isomer or of the parent base in water or in 0.1 *N* sodium hydroxide exhibited maxima in mμ at 327, 314, 302, 289, 238, and 224 (log ε 3.96, 4.08, 3.99, 4.03, 4.11, and 4.08). Solutions in 0.1 *N* hydrochloric acid exhibited maxima in mμ at 328, 314, 305 (shoulder), 243, and 220 (log ε 4.24, 4.27, 4.08, 4.14, and 4.24).

Chloroform solutions of the isomers showed dissimilar infrared absorption in the 6.1–7-μ region and each showed well developed bands at 3.41, 7.30, and 7.55 μ. Isomer A could be differentiated by well developed maxima at 8.75, 10.30, 10.45, 10.60, and 10.85 μ which were lacking in isomer B. In potassium bromide disks, both compounds possessed poorly differentiated bands in the 3-μ region, with maxima at 2.95 μ.

Reduction of 4-(1-Methyl-1-oxo-3-pyrrolidinylmethylamino)quinazolines to 4-(1-Methyl-3-pyrrolidinylmethylamino)quinazoline.—Solutions of 12.9 g. (0.05 mole) of the oxides in 50 ml. of ethyl alcohol were shaken with 10% palladium-on-carbon under hydrogen in a Parr machine. One equivalent of hydrogen was absorbed in 20 min. after which absorption stopped. After removal of catalyst the solutions were concentrated and the residues recrystallized from acetonitrile to furnish quantitative yields of 4-(1-methyl-3-pyrrolidinylmethylamino)quinazoline. The latter was identified by comparison of melting points (112°) and infrared spectra with authentic material.

Dimethylaniline Color Reaction.[4]—A mixture of 0.1 g. of the oxide, 0.05 ml. of concd. hydrochloric acid, and 0.2 ml. of dimethylaniline was boiled in a test tube for 1 min. An intense blue color was obtained on the addition of ethyl alcohol to the cooled residue.

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Succinamoyl Azide. Preparation and Some Reactions

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For studies on cyclic diacyl diimides,[1] a variety of cyclic diacyl hydrazides were required to serve as precursors in their preparations. Unfortunately, many cyclic diacyl hydrazides are unstable relative to isomeric polymers, and cannot be prepared by interactions of the appropriate diacyl derivatives with hydrazine. For this reason it was of interest to find a general synthetic method in which cyclic diacyl hydrazides would be produced in rate-controlled processes under conditions unfavorable for subsequent isomerizations. In view of recent work on the intermediacy of monovalent azenes in some organic reactions,[2–4] it seemed possible that such a method would be that represented by the sequence of equation 1. The preparation of cyclic succinic hydrazide (1,2,4,5-tetrahydro-3,6-pyridazinedione) appeared a desirable one for testing this possibility, since its properties are known, and it is an example of a cyclic diacyl hydrazide which is unstable relative to isomeric polymers.[5] Unfortunately, when succinamoyl azide (**2**) was subjected to thermal or ultraviolet irradiative decomposition, there was no indication of the formation of cyclic succinic hydrazide; only products of normal Curtius rearrangement were observed. However, the preparation and characterization of the hitherto-unknown succinamoyl azide are of some interest and constitute the subject of this paper.

Succinamoyl azide (**2**) was prepared in 57% yield by the interaction of succinamoyl hydrazide (**1**)[6] with a molar equivalent of nitrosyl chloride

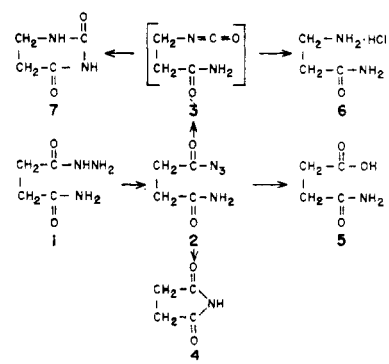

Fig. 1.—Some structures from, and reactions of, succinamoyl azide

in 1,2-dimethoxyethane, as solvent. It is a white crystalline material which, although isolable, is unstable, decomposing slowly at room temperature and almost explosively at *ca.* 70°. In the infrared it exhibited the characteristic azide absorption at 2150 cm.$^{-1}$.

Hydrolysis of succinamoyl azide (**2**) in the presence of two molar equivalents of sodium hydroxide, followed by acidification, produced succinamic acid (**5**) in 80% yield; however, when one molar equivalent of sodium hydroxide was employed, the only isolable product was succini-

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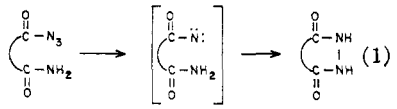

(1)

mide (4). Since succinamic acid (as its salt) is produced from succinimide by aqueous sodium hydroxide,[7] these observations suggest that the initial reaction of base with succinamoyl azide involves the formation of succinimide, directly, in a concerted, cyclic, neutralization process; the succinimide thus formed would produce succinamic acid (as its salt) in subsequent reaction with additional base. By contrast, when the hydrolysis of succinamoyl azide was attempted in aqueous hydrochloric acid, Curtius rearrangement intervened, gas (60% of theory for two moles—nitrogen plus carbon dioxide) was evolved, and β-alanine amide hydrochloride (6) was obtained in 51% yield as the only identifiable product.

The decomposition of pure succinamoyl azide (2) in a gas-measuring system occurred, almost explosively, at 72°, the increase in volume amounting to 98% of theory for the liberation of one molar volume of gas. Controlled decomposition of succinamoyl azide was accomplished at 80° in solution in 1,2-dimethoxyethane. When solvent was evaporated immediately after gas evolution had ceased, there was obtained β-isocyanatopropionamide (3) as a semisolid material, the structure of which was inferred from its infrared spectrum which exhibited $-NH_2$ absorption at 3300 and 3160 cm.$^{-1}$ and isocyanate absorption at 2270 cm.$^{-1}$. β-Isocyanatopropionamide (3) proved to be too labile for purification and characterization, decomposing to a complex mixture of products at room temperature and even in solution. From one such complex mixture of products obtained from 3 in 1,2-dimethoxyethane at room temperature, dihydrouracil (7) was isolated in 21% yield as the only identifiable substance. The yield of dihydrouracil was increased to 71% when the decomposition of succinamoyl azide was carried out as above and trimethylamine was added to the solution immediately after gas evolution had ceased. Further confirmation of the Curtius rearrangement product, β-isocyanatopropionamide, as the major product in the decomposition of succinamoyl azide was obtained by adding the solution, immediately after decomposition was complete, to cold aqueous hydrochloric acid; β-alanine amide hydrochloride (6) was obtained in 76% yield.

The decomposition of succinamoyl azide (2) was also accomplished by ultraviolet irradiation. The complex mixture of products thus obtained proved to be identical (infrared spectral comparison) with that from the thermal decomposition.

In none of the decompositions of succinamoyl azide (2) was there any indication of the formation of cyclic succinic hydrazide as judged by infrared spectral examination of the crude decomposition product. Intense absorption by cyclic succinic hydrazide at 2870 and 955 cm.$^{-1}$ were those absorptions most frequently conspicuous by their absence.

Thus, products from the thermal and ultraviolet irradiative decompositions of succinamoyl azide provide no evidence for the intermediacy of an acyl azene. If acyl azenes are involved in the decompositions of acyl azides,[8] they apparently lead always to normal Curtius rearrangement products.[8,9]

Experimental[10]

Succinamoyl Azide (2).—To a flask containing nitrosyl chloride (2.46 g., 37.6 mmoles) in 1,2-dimethoxyethane (200 ml.) and immersed in an ice bath was added succinamoyl hydrazide[6] (4.92 g., 37.5 mmoles). The slurry was stirred until the solution became colorless and most of the succinamoyl hydrazide had gone into solution (*ca.* 20 min.), when the flask was removed from the ice bath, anhydrous potassium carbonate (*ca.* 5 g.) was added, and the mixture was stirred until it had warmed to room temperature. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure at a temperature below 25° until solid appeared. At this point ether (300 ml.) was added and the solid was filtered, care being taken to leave a small oily residue in the flask. The solid was taken up in methylene chloride (500 ml.), the solution was filtered, and the filtrate was concentrated under reduced pressure at a temperature less than 25° to a volume of *ca.* 50 ml. Filtration yielded succinamoyl azide (2) as glistening white leaflets, dec. 70–80°. In the infrared, 2 exhibited absorption (potassium bromide pellet) at 3365 and 3180 ($-NH_2$), 2280 (weak, $-N{=}C{=}O$?), 2150 ($-N_3$), 1706 (azide acyl), and 1656 (amide acyl) cm.$^{-1}$; and (2% in chloroform) at 3520 and 3400 ($-NH_2$), 2150 ($-N_3$) and 1691 (broad, both acyl functions) cm.$^{-1}$.

Anal. Calcd. for $C_4H_6N_4O_2$: C, 33.80; H, 4.26. Found (after 1 hr.): C, 34.20; H, 4.36. Found (after 24 hr.): C, 35.86; H, 4.80.

Succinamoyl azide decomposes slowly at room temperature, and in the subsequent experiments it was employed immediately after preparation.

Hydrolysis of Succinamoyl Azide (2). (A). With Two Moles of Sodium Hydroxide.—A solution of succinamoyl azide (1.42 g., 10.0 mmoles) in 0.200 *N* sodium hydroxide (100 ml., 20.0 mmoles) was permitted to remain at room temperature for 24 hr. Hydrochloric acid (40 ml., 0.500 *N*, 20.0 mmoles) and silicic acid–Celite (5 g., 1:1 mixture) were added, and water was evaporated under reduced pressure to yield a free-flowing powder which was packed on top of a chromatographic column of silicic acid–Celite (30 g., 1:1 mixture). The column was developed with methanol–carbon tetrachloride mixtures, succinamic acid (5) (0.94 g., 80%), m.p. 148–150°, being eluted with 20% methanol in carbon tetrachloride. This material, by the criteria of mixture melting point and infrared spectral comparison, was identical with authentic succinamic acid,[7] m.p. 155–156° (lit.[7] m.p. 156–157°), which exhibited infrared absorption (potassium bromide pellet) at 3370, 3240, 2910, and

(7) R. Serda and J. Wiedemann, *Ber.*, **23**, 3284 (1890).

(8) K. R. Brower, *J. Am. Chem. Soc.*, **83**, 4370 (1961).

(9) C. R. Hauser and S. W. Kantor, *ibid.*, **72**, 4284 (1950).

(10) Melting points were determined on a calibrated Fisher-Johns apparatus. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer. I am indebted to Mr. W. Saschek of this department for the elemental analyses.

2570 (—H stretching), 1722 (carboxyl acyl), and 1645 (amide acyl) cm.$^{-1}$.

(B). **With One Mole of Sodium Hydroxide.**—Reaction and product isolation was as above except that 0.71 g. (5.00 mmoles) of succinamoyl azide and 25 ml. (5.00 mmoles) of 0.200 *N* sodium hydroxide were employed and that no acid was added prior to chromatography. Succinimide (4) (0.27 g., 54%), m.p. 121–124°, was eluted with 10% ethanol in carbon tetrachloride, as proved by mixture melting point and infrared spectral comparison with authentic succinimide, m.p. 123–125°.

(C). **With Hydrochloric Acid.**—A mixture of succinamoyl azide (1.19 g., 8.38 mmoles) and hydrochloric acid (40 ml., 0.200 *N*, 8.00 mmoles) was stirred at room temperature in a constant pressure gas-measuring apparatus for 23 hr., at the end of which time the evolution of gas (10.1 mmole, 60% of theory for two moles) was complete. Isolation was by chromatography as above, and β-alanine amide hydrochloride (6) (0.53 g., 51% on 2), m.p. 146–148°, was eluted with 50% methanol in carbon tetrachloride. A single crystallization from ethanol afforded pure 6 as white leaflets, m.p. 149–150° (lit.[11,12] m.p. 149°) which exhibited infrared absorption (potassium bromide pellet) at 3360, 3165, 3125, 3000, and 2945 (—H stretching) and 1669 (amide acyl) cm.$^{-1}$.

Thermal Decomposition of Succinamoyl Azide (2). (A). **Pure.**—When 2 (0.327 g., 2.30 mmoles) was warmed in a constant pressure gas-measuring apparatus, vigorous decomposition occurred at 72° and decomposition product was scattered throughout the apparatus. The increase in volume corresponded to 2.24 mmoles (98% of theory for one mole) of gas. A portion of the decomposition product which was recovered showed infrared absorption (potassium bromide pellet) at 3340 (s), 3160 (s), 3060 (m), 2860 (w), 1740 (s), 1685 (s), and 1650 (s) cm.$^{-1}$.

(B). **In 1,2-Dimethoxyethane.**—A solution of 2 (1.05 g.) in 1,2-dimethoxyethane (50 ml.) was heated under reflux until gas evolution ceased (*ca.* 10 min.). Solvent was immediately removed under reduced pressure and at room temperature to yield a semisolid material, presumed to be β-isocyanatopropionamide (3), which exhibited infrared absorption (potassium bromide pellet) at 3370 (s), 3160 (m), 2920 (w), 2270 (s), 1740 (m), and 1655 (s) cm.$^{-1}$. After three days this material had an infrared spectrum virtually identical with that of the decomposition product in (A).

When the decomposition of 2 (0.88 g., 6.2 mmoles) was carried out in 1,2-dimethoxyethane (100 ml.) as above, and the solution was permitted to remain at room temperature for 108 hr., there was obtained, after removal of solvent at reduced pressure, a white solid which had an infrared spectrum similar to that of the decomposition product in (A). From chromatography of this white solid on silicic acid–Celite (30 g., 1:1 mixture) there was obtained dihydrouracil (7) (0.15 g., 21%), eluted with 10% methanol in carbon tetrachloride, and identical by the criterion of infrared spectral comparison with authentic 7.[13] Authentic 7 had m.p. 276–278° (lit.[13] m.p. 272–275°) and exhibited absorption in the infrared (potassium bromide pellet) at 3220, 3070, and 2880 (—H stretching); 1740 (broad, acyl); and 1693 (sharp, acyl) cm.$^{-1}$.

(C). **In 1,2-Dimethoxyethane with Addition of Trimethylamine.**—A solution of 2 (1.59 g., 11.2 mmoles) in 1,2-dimethoxyethane (100 ml.) was decomposed as in B), the solution was cooled, and to it was added trimethylamine (7 g.). After 12 hr. at room temperature, during which time solid crystallized from solution, the total mixture was evaporated under reduced pressure to yield a white solid (1.33 g., 108% of theory for loss of nitrogen gas) which was chromatographed on silicic acid–Celite (60 g., 1:1 mixture). Dihydrouracil (7) (0.90 g., 71% on 2), m.p. 257–271°, was eluted with 40% methanol in carbon tetrachloride, and was identical, by the criteria of mixture melting point and infrared spectral comparison, with the authentic sample of 7 described in (B).

(D). **In 1,2-Dimethoxyethane with Addition to Hydrochloric Acid.**—A solution of 2 (1.08 g., 7.6 mmoles) in 1,2-dimethoxyethane (100 ml.) was decomposed as in (B), cooled, and stirred into iced hydrochloric acid (10.0 mmoles). Silicic acid–Celite (5 g., 1:1 mixture) was added to the solution and the mixture was evaporated under reduced pressure to yield a free-flowing powder which was chromatographed as in (C). Elution of the column with 50% methanol in carbon tetrachloride afforded β-alanine amide hydrochloride (6) (0.72 g., 76%), m.p. 148–149°, identical, by the criteria of mixture melting point and infrared spectral comparison with the sample of pure 6 described above.

Irradiative Decomposition of Succinamoyl Azide (2).—A slurry of 2 (1.00 g.) in methylene chloride (100 ml.) was stirred in an irradiation apparatus fitted with a reflux condenser and, internally, with a Hanovia 54 A 36 S high pressure mercury lamp. Irradiation, in a nitrogen atmosphere and under vigorous reflux, was continued for 14 hr., when a sample of the product showed no infrared absorption in the 2100–2300-cm.$^{-1}$ region. By evaporation of the reaction mixture, there was obtained a white solid which had an infrared spectrum identical with that of the thermal decomposition product described in (B) above.

Acknowledgment.—I am indebted to the U. S. Army Research Office (Durham) for support of this research under Grant DA-ORD-31-124-61-G86.

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Synthesis of Analgesics with Benzomorphane Structure. A Possible Intermediate: 1-Methyl-2-benzyl-4-piperidol

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In the course of investigations concerning the synthesis of analgesics of the benzomorphane series it became of interest to prepare the intermediate 1-methyl-2-benzyl-4-piperidol (VII).

The following method of synthesis gave excellent results. Phenylacetaldehyde was condensed with monoethyl malonate as described by Moureau[2] to give ethyl 4-phenyl-2-butenoate in 65% yield. This ester, by treatment with methylamine as described by Morsch[3] for the reaction between methylamine and crotonic acid, was converted into *N*-methyl-3-methylamino-4-phenylbutyramide (I), which was in turn hydrolized to the free acid II. II was esterified giving ethyl 3-methylamino-

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