yielded 32.7 g. (75%) of an orange-yellow liquid, b.p. 107–108° (5 mm.). This liquid yielded small, bright yellow needles when its ethanol solution was chilled in an ice–salt-bath. Three recrystallizations carried out in the same manner gave a product of m.p. 27°.

Anal. Calcd. for $C_6H_2NO_2F_2I$: C, 25.28; H, 0.70. Found: C, 25.49; H, 0.78.

4,4',6,6'-Tetrafluoro-2,2'-dinitrobiphenyl.—A mixture of 30 g. of 2,5-difluoro-6-nitroiodobenzene and 30 g. of copper powder (O. B. Hommel Co., No. 1 Extra Fine, No. 5743) was heated to 115°, when the temperature rose suddenly to 260° and then declined. The cooled mixture was extracted with boiling acetone, which was then replaced with ethanol. The hot solution was treated with two portions of decolorizing charcoal, and then the bright yellow solution when cooled yielded 10.0 g. of a yellow solid, m.p. 72–77°. Another 2.5 g. of the same compound (75% total yield) separated when the mother liquors were concentrated. Recrystallization from ethanol gave bright yellow plates, m.p. 78.5–80°.

Anal. Calcd. for $C_{12}H_4N_2O_4F_4$: C, 45.59; H, 1.26. Found: C, 45.58; H, 1.43.

2,2'-Diamino-4,4',6,6'-tetrafluorobiphenyl (IV).—A solution of 7.2 g. of 4,4',6,6'-tetrafluoro-2,2'-dinitrobiphenyl in hot ethanol was treated with 2 g. of Raney nickel and then with hydrogen under three atmospheres pressure at room temperature. The filtered solution was treated with three portions of decolorizing charcoal. Dilution of the solution with water caused the separation of 5.8 g. (~100%) of pale pink needles, m.p. 92–94°. This substance was converted after two recrystallizations from ethanol into tiny needles, m.p. 100–101°.

Anal. Calcd. for $C_{12}H_8N_2F_4$: C, 56.27; H, 3.12. Found: C, 56.30; H, 3.10.

The N,N'-diacetyl derivative was prepared in 83% yield by treating an ether solution of IV with ketene until precipitation of the white solid derivative, m.p. 209.5–211°, was complete. Recrystallization from aqueous ethanol gave tiny white needles of the same m.p.

Anal. Calcd. for $C_{16}H_{12}N_2O_2F_4$: C, 56.47; H, 3.56. Found: C, 56.61; H, 3.63.

The N,N'-bis-salicylal derivative was obtained by boiling a solution of 0.2 g. of IV with 3 ml. of salicylaldehyde for 15 minutes. The hot solution was treated with 8 ml. of ethanol and then with water until a faint cloudiness appeared. Cooling caused the separation from the solution of 0.3 g. (83%) of yellow crystals, m.p. 181–184°. The derivative formed bright yellow needles, m.p. 183–184°, after two recrystallizations from benzene–petroleum ether (b.p. 30–60°).

Anal. Calcd. for $C_{26}H_{16}N_2O_2F_4$: C, 67.24; H, 3.48. Found: C, 67.03; H, 3.58.

1,3,10,12-Tetrafluoro-6,7-diphenyldibenzo[e.g.][1,4]-diazocine (VII).—A mixture of 5.16 g. of IV and 0.420 g. of benzil was heated for 30 minutes at 160–180°; then it was dissolved in glacial acetic acid and the solution was boiled. Cooling the solution caused the separation of black prisms, m.p. 197–198°, which were converted into bright yellow prisms, m.p. 199–200°, after four recrystallizations from ethanol.

Anal. Calcd. for $C_{26}H_{14}N_2F_4$: C, 72.56; H, 3.26; N, 6.51; mol. wt., 430.4. Found: C, 72.68; H, 3.46; N, 6.29; mol. wt. (Rast), 420.

The ultraviolet absorption spectrum showed a single broad band with its maximum at 262–264 mμ (log ε 4.46); this spectrum resembles that of benzil,[11] but not that of IV.

2,2'-Diaminobiphenyl, m.p. 78.5°, was prepared for spectroscopic examination by reducing[3] 2,2'-dinitrobiphenyl which, in turn, was obtained by the Ullmann coupling of *o*-iodonitrobenzene. This coupling was effected in 61% yield by heating 20 g. of *o*-iodonitrobenzene, 20 g. of copper powder and 40 g. of clean sand to 130°. At this point the temperature of the mixture rose to 210° and then dropped. The cooled mixture was extracted with boiling benzene, the benzene solution was concentrated and diluted with petroleum ether (b.p. 65–110°), and the solution was cooled. The product separated in bright yellow flakes, m.p. 124–125°. The reported[12] m.p. is 124°.

Treatment of Hydrazobenzene with 2:1 Sulfuric Acid.—The same general procedure was applied to the reaction of hydrazobenzene with 2:1 sulfuric acid at 85–90° as had been applied to the tetrafluoro analog. The medium-insoluble solids yielded, by the same procedures, azobenzene and benzidine. The product solution, again by use of parallel procedures, yielded acetanilide and a residue from the steam distillation of the aniline which was extracted with ether. The ether solution was treated with acetic anhydride, and N,N'-diacetyldiphenyline was obtained by removing the ether and pouring the residue into water. All products were identified by their melting points. Yields of products were reported in the Discussion section.

Ultraviolet absorption spectra were determined in 95% ethanol[13] solution by means of a Beckman quartz spectrophotometer, Model DU.

PITTSBURGH 13, PENNSYLVANIA

(11) L. C. Anderson and M. J. Roedel, THIS JOURNAL, **67**, 956 (1945).

(12) H. C. Gull and E. E. Turner, *J. Chem. Soc.*, 494 (1929).

(13) Stock 95% ethanol found to be indistinguishable in the spectrophotometer from ethanol purified by the method of P. A. Leighton, R. W. Crary and L. T. Schipp, THIS JOURNAL, **53**, 3017 (1931).

[CONTRIBUTION FROM EATON LABORATORIES, DIVISION OF THE NORWICH PHARMACAL COMPANY]

Chemotherapeutic Nitrofurans. I. Some Derivatives of 3-Amino-2-oxazolidone[1]

BY GABRIEL GEVER, CHARLES O'KEEFE, GORDON DRAKE, FRANK EBETINO, JULIAN MICHELS AND KENYON HAYES

RECEIVED NOVEMBER 22, 1954

A number of 3-amino-2-oxazolidones have been prepared by the cyclization of 2-(2-hydroxyalkyl)-semicarbazides with hydrochloric acid, the condensation of β-hydrazino alcohols with some carbonic acid esters and chlorides and the catalytic or electrolytic reduction of 3-nitro-2-oxazolidones. These 3-amino-2-oxazolidone have been converted to chemotherapeutically active 5-nitro-2-acylfuran derivatives.

During the investigation of the preparation of substituted semicarbazides[2] it became of interest to prepare 2-(2-hydroxypropyl)-semicarbazide. An aqueous solution of 1-hydrazino-2-propanol hydrochloride was treated with potassium cyanate and after cyanation was deemed complete the solution was acidified. Treatment of this aqueous solution with 5-nitro-2-furaldehyde gave the expected 5-nitro-2-furaldehyde 2-(2-hydroxypropyl)-semicarbazone. In an attempt to isolate 2-(2-hydroxypropyl)-semicarbazide hydrochloride, part of the original cyanation solution was concentrated *in vacuo*, leaving a gummy residue. Since no crystalline solid was obtained, the residue was taken up in water and treated with 5-nitro-2-furaldehyde.

(1) Part of the material in this paper is the subject of U. S. Patent 2,652,402, Sept. 15, 1953 (*C. A.*, **48**, 12179d (1954)).

(2) G. Gever and K. Hayes, *J. Org. Chem.*, **14**, 813 (1949).

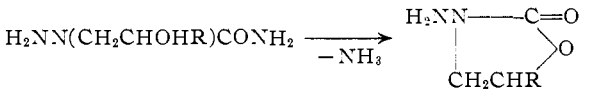
From the resulting precipitate were isolated two solids, 5-nitro-2-furaldehyde 2-(2-hydroxypropyl)-semicarbazone, m.p. 195°, and the other an unknown substance of m.p. 255°.

An elementary analysis of the unknown material corresponded to a compound formed by the loss of one mole of ammonia from the hydroxypropyl semicarbazone.

Refluxing a strongly acidic solution of 2-(hydroxyethyl)-semicarbazide followed by addition of 5-nitro-2-furaldehyde or benzaldehyde resulted in the formation of compounds whose composition also corresponded to the loss of ammonia from the corresponding 2-(hydroxyethyl)-semicarbazones.

Bacteriological screening[3] showed that these 5-nitro-2-furaldehyde derivatives had a high order of activity so it became of extreme interest to determine their structures.

A hypothesis which seemed reasonable was the formation of a 3-amino-2-oxazolidone from the corresponding 2-(2-hydroxyalkyl)-semicarbazide, *i.e.*



A search of the literature revealed that only one derivative of a 3-amino-2-oxazolidone had been reported. Paterno and Cingolani[4] nitrated 5-chloromethyl-2-oxazolidone and reduced the 3-nitro compound with zinc and acetic acid. They were unable to isolate the free base but did characterize the benzaldehyde condensation product.

However, the cyclization of 2-hydroxyalkylureas, which differ from the hydroxyalkylsemicarbazides by an N-amino group, to give 2-oxazolidones is known. Knorr and Rossler[5] obtained 2-oxazolidone by distilling 2-hydroxyethylurea and Stratton and Wilson[6] prepared 4-methyl-5-phenyl-2-oxazolidone by cyanating *d*-nor-ψ-ephedrine sulfate to give the 2-hydroxyalkylurea and then heating the product.

The structure of the N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone was confirmed by the nitration of 2-oxazolidone[7] followed by reduction and condensation of the product with 5-nitro-2-furaldehyde. The compound obtained by this procedure was identical with that obtained from the heating of 2-(2-hydroxyethyl)-semicarbazide. By analogy, the structure of the product obtained from the 2-(2-hydroxypropyl)-semicarbazide was assumed to be N-(5-nitro-2-furfurylidene)-3-amino-5-methyl-2-oxazolidone.

This process of nitration followed by reduction (catalytic and/or electrolytic) of C-substituted 2-oxazolidones also was used to prepare several 3-amino-2-oxazolidone derivatives.

Reduction of nitramides in general has received little attention[8] and the only mention in the literature of the reduction of a 3-nitro-2-oxazolidone is the work of Paterno and Cingolani.[4]

The catalytic reductions were carried out at 1–3 atmospheres with solvent, temperature and nature of catalyst being varied. Reduction of 3-nitro-2-oxazolidone in the desired direction took place only in an acidic medium and with platinum oxide as a catalyst. Raney nickel in absolute alcohol, dioxane or methanolic potassium hydroxide gave none of the desired product. Palladium-on-charcoal (5%) in absolute alcohol, dioxane, acetic acid or dilute hydrochloric acid likewise gave no 3-amino-2-oxazolidone, but considerable amounts of 2-oxazolidone were isolated.

The reduction of 3-nitro-2-oxazolidone with platinum oxide was carried out in several dilute acids. Best results were obtained in dilute hydrochloric acid; dilute sulfuric, acetic or oxalic acids were markedly inferior. The concentration of hydrochloric acid was found to be significant in that with a given batch of catalyst a maximum yield was obtained over a small range (0.5–2.5 *N*) of acid concentration. It could well be that for this reduction to proceed as desired, the catalyst must be mildly poisoned. This would explain the superiority of hydrochloric acid since it is known that halogen acids are mild poisons for noble metal catalysts.[9] Slight batch differences in the starting platinum oxide would then account for the shift of optimum acid concentration.

The yield of 3-amino-2-oxazolidone was found to increase with decreasing temperature, 5, 12, 17 and 55% being obtained at temperatures of 50, 30, 24 and 2°, respectively. This observation is consistent with that of Lieber and Smith[10] for the catalytic reduction of nitroguanidine. Variation of the pressure in the range of one to three atmospheres had no effect on the yield.

The reduction of 4,4-dimethyl-3-nitro-2-oxazolidone in hydrochloric acid with platinum oxide gave a better yield of 3-amino-4,4-dimethyl-2-oxazolidone.

A series of electrolytic reductions of 3-nitro-2-oxazolidone was carried out varying the current density, the cathode, the catholyte and temperature. Mercury, tinned copper and aluminum were tried as cathodes, with mercury proving to be by far the best. A 10% sulfuric acid solution was found to be the most satisfactory catholyte. Attempts to increase the solubility of the 3-nitro-2-oxazolidone by adding acetic acid, acetone or alcohol resulted in decreased yields. Increasing the temperature also resulted in lower yields. Using a mercury cathode and 10% sulfuric acid as the catholyte, the yield of 3-amino-2-oxazolidone increased proportionally with an increase in current density up to approximately 0.2 amp./cm.^{2} above which it tapered off. The filtrate remaining after the N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone had been isolated was examined in several instances and an amount of 2-oxazolidone recovered therefrom which represented a large percentage of the starting material. This was

(3) J. Yurchenco, M. Yurchenco and C. Piepoli, *Antibiotics & Chemotherapy*, **3**, 1040 (1953).

(4) E. Paterno and E. Cingolani, *Gazz. chim. ital.*, [1] **38**, 243 (1908).

(5) L. Knorr and P. Rossler, *Ber.*, **36**, 1278 (1903).

(6) J. Stratton and F. Wilson, *J. Chem. Soc.*, 1133 (1932).

(7) A. Franchimont and A. Lublin, *Rec. trav. chim.*, **21**, 45 (1902).

(8) (a) A. Lamberton, *Quart. Revs.*, **5**, 75 (1951); (b) H. Backer, *Rec. trav. chim.*, **31**, 1 (1912).

(9) J. Houben, "Die Methoden der Organischen Chemie" (Reprint Edition) Edwards Brothers, Inc., Ann Arbor, Michigan, 1943, p. 500.

(10) E. Lieber and G. Smith, THIS JOURNAL, **58**, 2170 (1936).

proven to be the product of a competing reaction rather than a further reduction of the desired product since 3-amino-2-oxazolidone was not reduced under these conditions.

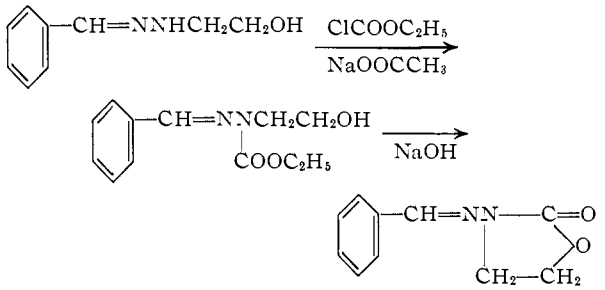
Electrolytic reductions were carried out in a similar manner on the corresponding nitro compounds to prepare 3-amino-5-chloromethyl-2-oxazolidone[4] and 3-amino-4,4-dimethyl-2-oxazolidone.

It is known that 2-oxazolidones can be prepared from ethanolamines and diethyl carbonate,[11] ethyl chlorocarbonate[12] and phosgene.[13] It was found that the reaction of β-hydrazino alcohols with these carbonic acid derivatives yielded 3-amino-2-oxazolidones.

Diethyl carbonate was heated with the appropriate hydrazino alcohol in the presence of sodium methoxide, either refluxing the mixture or slowly distilling the ethanol formed in the reaction. With 2-hydrazinoethanol and 1-hydrazino-2-propanol, the corresponding 3-amino-2-oxazolidone and 3-amino-5-methyl-2-oxazolidone separated as crystalline solids. The other alkylated 3-amino-2-oxazolidones were characterized as derivatives of 5-nitro-2-furaldehyde. The yields of the 3-amino-2-oxazolidones varied from 20 to 79% depending on the nature of the starting hydrazino alcohol (see Table II).

The method of preparing 3-amino-5-hydroxymethyl-2-oxazolidone, which utilized 1-hydrazino-2,3-dihydroxypropane as the starting material, might have produced 3-amino-5-hydroxytetrahydro-1,3-oxazine-2-one, or a mixture of the two N-aminoheterocycles. Therefore, the 5-nitro-2-furaldehyde derivative of the presumed 3-amino-5-hydroxymethyl-2-oxazolidone was treated with thionyl chloride to give a product which was identical with the material obtained by treating 5-nitro-2-furaldehyde with 3-amino-5-chloromethyl-2-oxazolidone prepared by the method of Paterno and Cingolani.[4]

Ethyl chlorocarbonate when treated directly with 2-hydrazinoethanol gave only a 15% yield of the desired 3-amino-2-oxazolidone. Since it seemed probable that substitution was taking place on both nitrogen atoms of the hydrazinoethanol, the latter was first condensed with benzaldehyde and the product then treated with ethyl chlorocarbonate in the presence of sodium acetate. The



intermediate N-benzylidene-N′-carbethoxy-N′-(2-hydroxyethyl)-hydrazine so formed was cyclized with sodium hydroxide to give an 85% yield of N-benzylidene-3-amino-2-oxazolidone.

The sodium acetate in the above reaction serves to buffer the solution at a *p*H of 6–7. If the *p*H is higher than 9 or lower than 6 a lower yield is obtained. The optimum ratio of ethyl chlorocarbonate to benzaldehyde 2-hydroxyethylhydrazone was found to be 1.4:1.

As in the case of ethyl chlorocarbonate, it was found that the reaction of phosgene with 2-hydrazinoethanol gave much better results if the latter were first condensed with a carbonyl compound. Acetone 2-hydroxyethylhydrazone when treated with phosgene in acetone solution followed by the addition of 5-nitro-2-furaldehyde gave a 62% yield of N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone.

All the 3-amino-2-oxazolidones were converted to their 5-nitro-2-furaldehyde derivatives and in addition, some were condensed with 5-nitro-2-furanacrolein and methyl 5-nitro-2-furyl ketone and ethyl 5-nitro-2-furyl ketone. The new, chemotherapeutic nitrofurans obtained by this procedure are shown in Table I.

Experimental[14]

A. Acid Treatment of 2-(2-Hydroxyalkyl)-semicarbazides. N-(5-Nitro-2-furfurylidene)-3-amino-5-methyl-2-oxazolidone and 5-Nitro-2-furaldehyde 2-(2-Hydroxypropyl)-semicarbazone.—A solution of 58 g. of 1-hydrazino-2-propanol[15] in 300 cc. of water was adjusted to *p*H 7 with 20% hydrochloric acid. A solution of 60 g. of potassium cyanate in 75 cc. of water was added and the resulting solution allowed to stand at room temperature for three days. The solution was then acidified with hydrochloric acid, giving 590 cc. of a solution of 2-(2-hydroxypropyl)-semicarbazide hydrochloride.

To 90 cc. of this solution was added 60 cc. of water followed by a solution of 10 g. of 5-nitro-2-furaldehyde in 20 cc. of alcohol. The resulting precipitate was recrystallized from a mixture of 200 cc. of alcohol and 100 cc. of dioxane, yielding 7.9 g. of product, m.p. 193–195°. A sample of this material was recrystallized from dioxane, m.p. 195–196°. The solubility in water at 25° is 600 mg./l. Ultraviolet absorption maxima in water occurred at 3850 and 2700 Å., E_M = 16,100 and 12,400, respectively.

Anal. Calcd. for $C_9H_{12}N_4O_5$: C, 42.19; H, 4.72. Found: C, 42.07; H, 4.82.

Three hundred and sixty cc. of the original solution was concentrated at 15 mm. to a gummy solid. This material was dissolved in 150 cc. of water and treated with a solution of 10 g. of 5-nitro-2-furaldehyde in 15 cc. of alcohol. The yellow solid which precipitated was filtered, washed with water and dried; 18 g., m.p. 185–210°. The 18 g. was boiled with 100 cc. of dioxane and filtered hot, leaving some insoluble material which melted at 250–255°. The filtrate upon cooling deposited 7.0 g. of yellow solid, m.p. 193–195°, which proved to be identical with the 5-nitro-2-furaldehyde 2-(2-hydroxypropyl)-semicarbazone above.

The insoluble material was recrystallized from 500 cc. of dioxane giving 5.0 g. of yellow solid, m.p. 255°. Recrystallization from 50% acetic acid did not change the melting point. The same compound was obtained by refluxing a strongly acidified solution of 2-(2-hydroxypropyl)-semicarbazide for four hours and treating the resulting solution with 5-nitro-2-furaldehyde.

2-(2-Hydroxyethyl)-semicarbazide.[16]—To a solution of

(11) A. Homeyer, U. S. Patents 2,399,118, April 23, 1946 (*C. A.*, **40**, 4084[6] (1946)); 2,437,388, 2,437,389 and 2,437,390, March 9, 1948 (*C. A.*, **42**, 4613*g* (1948)).

(12) V. Ettel and V. Weichet, *Coll. Czech. Chem. Communs.*, **13**, 316 (1948); J. Cason and F. Prout, THIS JOURNAL, **71**, 1218 (1949).

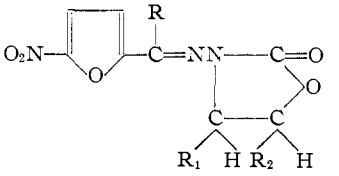
(13) P. Otto, *J. prakt. Chem.*, [2] **44**, 17 (1891); H. Crowther and H. Macombie, *J. Chem. Soc.*, **103**, 27 (1913); S. Frankel and M. Cornelius, *Ber.*, **51**, 1654 (1920).

(14) All melting points were taken on a Fisher–Johns apparatus and are corrected. We are indebted to Mr. Joseph Corrado for the analytical results.

(15) G. Gever, THIS JOURNAL, **76**, 1283 (1954).

(16) For the preparation of an aqueous solution of 2-(2-hydroxyethyl)-semicarbazide see U. S. Patent 2,416,234, Feb. 18, 1947 (*C. A.*, **41**, 3488i (1947)).

TABLE I



R	R_1	R_2	M.p., °C.	Empirical formula	Analyses, % Calcd. C	H	N	Found C	H	N	Molar absorption in water ϵ_{max}	$m\mu$
H	H	H	255	$C_8H_7N_3O_5$	42.67	3.14	18.66	42.97	2.96	18.77	16,800	367
H	H	CH_3	255	$C_9H_9N_3O_5$	45.19	3.79	17.57	45.43	3.80	17.11	16,400	365
H	CH_3	H	200	$C_9H_9N_3O_5$	45.19	3.79	17.57	45.07	3.85	17.31	16,200	367.5
H	n-C_4H_9	H	151	$C_{12}H_{15}N_3O_5$	51.24	5.38	14.94	51.44	5.13	15.08	16,500	367.5
H	H	n-C_4H_9	194	$C_{12}H_{15}N_3O_5$	51.24	5.38	14.94	51.42	5.30	15.16	17,200	367.5
H	H	CH_2Cl	196–197	$C_9H_8ClN_3O_5$	39.50	2.95	12.96[a]	39.62	3.05	13.30[a]	16,200	364
H	H	CH_2OH	242–243	$C_9H_9N_3O_6$	42.36	3.53	16.47	42.10	3.65	16.51	15,300	367
H	H	C_2H_5	215–216	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.54	4.34	16.67	17,300	367.5
H	CH_3	CH_3	143–144	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.48	4.40	16.79	17,000	365
H	C_2H_5	H	142–143	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.26	4.55	16.58	16,500	367.5
H	$(CH_3)_2$[c]	H	151–153	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.67	4.07	16.42	16,000	367.5
CH_3	H	H	133	$C_9H_9N_3O_5$	45.19	3.79	17.59	45.15	3.59	17.78	10,600	350
CH_3	H	CH_3	120–122	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.51	4.34	16.37	11,200	350
C_2H_5	H	H	102	$C_{10}H_{11}N_3O_5$	47.43	4.38	16.59	47.58	4.61	16.60	10,300	345
H	H	CH_3	258–259	$C_{11}H_{11}N_3O_5$[b]	49.79	4.18	15.84	50.05	3.92	15.82	22,200	395
H	H	H	268–269	$C_{10}H_9N_3O_5$[b]	47.82	3.61	16.73	47.62	3.68	16.62	22,100	395

[a] Chlorine. [b] 5-Nitro-2-furylacrolein derivative. [c] 4,4-Dimethyl derivative.

38 g. of 2-hydrazinoethanol in 200 cc. of water was added a solution of 40.5 g. of potassium cyanate in 200 cc. of water and the reaction mixture allowed to stand at room temperature for 44 hours. The solution was neutralized with concentrated hydrochloric acid and the water removed at room temperature *in vacuo*. The residue was dried thoroughly *in vacuo* and extracted with hot absolute alcohol. The alcohol extract, upon cooling, deposited crystals, m.p. 98–102°. These were recrystallized from 100 cc. of absolute alcohol, giving 18.2 g., 31%, of 2-(2-hydroxyethyl)-semicarbazide, m.p. 110°.

Anal. Calcd. for $C_3H_9N_3O_2$: C, 30.24; H, 7.61. Found: C, 30.48; H, 7.70.

Treatment of an alcoholic solution of 2-(2-hydroxyethyl)-semicarbazide with concentrated hydrochloric acid gave a precipitate of the hydrochloride, m.p. 156°.

Anal. Calcd. for $C_3H_{10}ClN_3O_2$: Cl, 22.79. Found: Cl, 23.15.

N-(5-Nitro-2-furfurylidene)-3-amino-2-oxazolidone.—A solution of 10 g. of 2-(2-hydroxyethyl)-semicarbazide hydrochloride in 150 cc. of water and 50 cc. of concentrated hydrochloric acid was refluxed for 15 minutes, cooled and treated with a solution of 5 g. of 5-nitro-2-furaldehyde in 100 cc. of alcohol. A yellow solid precipitated which, after washing and drying, weighed 3.0 g., m.p. 240–255°. The 3.0 g. was recrystallized from 50 cc. of nitromethane, giving 2.3 g. of solid, m.p. 255°. Recrystallization from fresh nitromethane did not alter the melting point.

The use of benzaldehyde in place of 5-nitro-2-furaldehyde gave N-benzylidene-3-amino-2-oxazolidone, m.p. 142°.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.14; H, 5.30; N, 14.73. Found: C, 63.29; H, 5.01; N, 14.73.

B. **Catalytic and Electrolytic Reduction of 3-Nitro-2-oxazolidones. 2-Oxazolidones.**—2-Oxazolidone and 4,4-dimethyl-2-oxazolidone were prepared by the method of Homeyer[11] and 5-chloromethyl-2-oxazolidone by the method of Thomsen.[17]

3-Nitro-2-oxazolidones.—All the 2-oxazolidones were nitrated by the method of Franchimont and Lublin.[7] Both 3-nitro-2-oxazolidone[7] and 5-chloromethyl-3-nitro-2-oxazolidone[4] are known substances but 4,4-dimethyl-3-nitro-2 oxazolidone has not been reported previously. It melts at 124° after recrystallization from alcohol.

Anal. Calcd. for $C_5H_8N_2O_4$: C, 37.50; H, 5.03; N, 17.50. Found: C, 37.79; H, 4.69; N, 17.72.

(17) A. Thomsen, *Ber.*, **11**, 2136 (1878).

N-(5-Nitro-2-furfurylidene)-3-amino-2-oxazolidone.—The reductions were carried out either in a Parr–Burgess shaker at 2–3 atmospheres, or in three-necked flask with vigorous mechanical stirring at 0–5° and atmospheric pressure. The 3-nitro-2-oxazolidone was suspended in the solvent and hydrogenation carried on until absorption ceased. The catalyst was removed by filtration and an alcoholic solution of 5-nitro-2-furaldehyde added to the filtrate. The N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone was washed with water and alcohol and dried to constant weight. This product was identical in all respects with the compound obtained from the acid treatment of 2-(2-hydroxyethyl)-semicarbazide.

Hydrogenation, using platinum oxide[18] as a catalyst, with *N* sulfuric acid, *N* oxalic acid, 15% acetic acid or water as a solvent at 25° gave yields of 10, 6.5, 2 and 0%, respectively, as compared with a yield of 17% with *N* hydrochloric acid under the same conditions.

N-(5-Nitro-2-furfurylidene)-3-amino-4,4-dimethyl-2-oxazolidone.—A suspension of 8.0 g. of 4,4-dimethyl-3-nitro-2-oxazolidone in 90 cc. of 1 *N* hydrochloric acid was reduced as above at room temperature with 0.3 g. of platinum oxide. The excess catalyst and 3.0 g. of unreacted starting material were removed by filtration and an excess of an alcoholic solution of 5-nitro-2-furaldehyde added to the filtrate. The yield of N-(5-nitro-2-furfurylidene)-3-amino-4,4-dimethyl-2-oxazolidone was 5.3 g., 67%.

N-Benzylidene-3-amino-4,4-dimethyl-2-oxazolidone was prepared in an analogous manner and melted at 77.5–78.5°.

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.46. Found: C, 66.03; H, 6.43.

Electrolytic Reductions.—The following example will illustrate the procedure used for a typical reduction. Mercury covering the bottom of a 400-cc. beaker (7.5 cm. diameter) served as the cathode. The anode, a piece of lead sheet having approximately the same area as the cathode, was contained in a Coors porous porcelain cup to prevent reduced material from reaching it. The anolyte was 10% sulfuric acid. Into the beaker was placed 160 cc. of 10% sulfuric acid and 5 g. of 3-nitro-2-oxazolidone. The mixture was stirred and kept at 5–10° with a Dry Ice and kerosene-bath while the current (0.2 amp./cm.^{2}) was passed through. When the 3-nitro-2-oxazolidone had dissolved (one hour) the catholyte was treated with a solution of 5.5 g. of 5-nitro-2-furaldehyde in 15 cc. of alcohol. The precipitate was

(18) The platinum oxide was purchased from the American Platinum Works.

filtered, washed with water and alcohol to give 3.9 g., 43% of N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone.

In several experiments the filtrate was extracted with ether to remove excess 5-nitro-2-furaldehyde and the aqueous portion made basic with sodium carbonate solution. The solution was evaporated to dryness and the residue extracted with hot chloroform. The chloroform extracts were evaporated to dryness to yield up to 50% of 2-oxazolidone, m.p. 87–88°, after recrystallization from benzene.

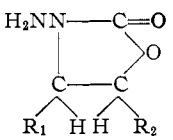
Using a similar procedure, 5-chloromethyl-3-nitro-2-oxazolidone and 4,4-dimethyl-3-nitro-2-oxazolidone were reduced to the corresponding 3-amino-2-oxazolidones in yields of 20 and 45%, respectively. Because of the low solubility of these nitroöxazolidones the time of reaction was appreciably longer than that required for 3-nitro-2-oxazolidone.

C. Condensation of β-Hydrazino Alcohols with Carbonic Acid Derivatives. Hydrazinoalcohols.—2-Hydrazinoethanol was prepared by the method of Gever and O'Keefe.[19] The other hydrazino alcohols were obtained by the method of Gever.[15]

Reactions of Hydrazino Alcohols with Diethyl Carbonate.—Since the 3-amino-2-oxazolidones were prepared by an identical procedure, only one example will be presented in detail. Table II gives the yields obtained in each case, these yields being based on the amount of the 5-nitro-2-furaldehyde derivative isolated.

TABLE II

YIELDS OF 3-AMINO-2-OXAZOLIDONES OBTAINED FROM THE REACTION OF β-HYDRAZINO ALCOHOLS WITH DIETHYL CARBONATE



R_1	H	H	CH_3	C_4H_9	H	C_2H_5	H	CH_3	CH_2OH
R_2	H	CH_3	H	H	C_4H_9	H	C_2H_5	CH_3	H
Yield, %	79	70	36	46	42	62	20	45	34

A mixture of 1.8 g. (0.08 mole) of sodium in 25 cc. of anhydrous methanol, 46 g. (0.63 mole) of 2-hydrazinoethanol and 88 g. (0.74 mole) of diethyl carbonate was refluxed for three hours and cooled to room temperature. The solution was diluted with 375 cc. of ethanol and acidified with 25 cc. of concentrated hydrochloric acid. To the resulting solution was slowly added, with stirring, a solution of 75 g. of 5-nitro-2-furaldehyde in 750 cc. of ethanol. The mixture was filtered and the yellow solid washed well with water and alcohol.

Two of the free bases, 3-amino-2-oxazolidone and 3-amino-5-methyl-2-oxazolidone, were obtained as crystalline solids directly from the reaction mixture and were characterized *per se*.

3-Amino-2-oxazolidone. *Anal.* Calcd. for $C_3H_6N_2O_2$: C, 35.29; H, 5.92; N, 27.44. Found: C, 35.30; H, 5.86; N, 27.57.

3-Amino-5-methyl-2-oxazolidone. *Anal.* Calcd. for $C_4H_8N_2O_2$: C, 41.37; H, 6.94; N, 24.13. Found: C, 41.00; H, 6.90; N, 24.15.

Although 3-amino-4,5-dimethyl-2-oxazolidone did not solidify, it formed a crystalline neutral oxalate salt, m.p. 125–126° (from alcohol).

Anal. Calcd. for $C_5H_{10}N_2O_2 \cdot {}^1/_2C_2H_2O_4$: C, 41.14; H, 6.33; N, 16.00. Found: C, 41.54; H, 6.70; N, 16.33.

Reaction of 2-Hydrazinoethanol with Ethyl Chlorocarbonate.—To a solution of 10.0 g. (0.13 mole) of 2-hydrazinoethanol in 48 cc. of water was added with stirring a solution containing 14.8 g. (0.14 mole) of benzaldehyde in 40 cc. of ethanol. The addition time was 30 minutes, the temperature being maintained at 26–29°. After five minutes, 41.7 g. of sodium acetate was added all at once following which 19.9 g. (0.18 mole) of ethyl chlorocarbonate was added over a period of 80 minutes, keeping the temperature at 20–22°. The reaction mixture was stirred for 15 minutes and then a solution of 7.4 g. of sodium hydroxide in 50 cc. of water was added. After stirring at room temperature for one hour, the mixture was cooled and filtered to give 22.6 g., 90%, of crude N-benzylidene-3-amino-2-oxazolidone. Recrystallization from ethanol gave 21.2 g., 85%, of product melting at 143–145°.

Reaction of 2-Hydrazinoethanol with Phosgene.—To 50 g. of acetone was added 29 g. of 2-hydrazinoethanol, cooling the mixture with cold water. The excess acetone was removed and the residue distilled *in vacuo* to yield 42 g. of acetone 2-hydroxyethylhydrazone, b.p. 107–108° at 10 mm.

Anal. Calcd. for $C_5H_{12}N_2O$: C, 51.69; H, 10.42; N, 24.12. Found: C, 51.50; H, 10.60; N, 24.30.

Into a stirred solution of 12.4 g. (0.11 mole) of acetone 2-hydroxyethylhydrazone in 100 cc. of acetone was bubbled 8 g. (0.081 mole) of phosgene over a period of 20 minutes, keeping the temperature at 20–25°. The reaction was run in a closed system under a slight pressure so as to prevent loss of phosgene. After the addition was completed, the solution was stirred for two hours. The excess acetone was removed by distilling *in vacuo* and the residue dissolved in 200 cc. of warm water. After filtering to remove a small amount of insoluble material, a solution of 15 g. (0.11 mole) of 5-nitro-2-furaldehyde in 50 cc. of isopropyl alcohol was added. The resulting precipitate was removed by filtration, washed with water and isopropyl alcohol and dried to yield 11.3 g., 62%, of N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone, m.p. 255°.

5-Nitro-2-acylfuran Derivatives.—3-Amino-2-oxazolidone was condensed with 5-nitro-2-furaldehyde or 5-nitro-2-furylacrolein[20] in acidic aqueous medium to give quantitatively N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone, m.p. 255°, or N-[(5-nitro-2-furyl)-acrylal]-3-amino-2-oxazolidone. A mixture of 21.2 g. of N-benzylidene-3-amino-2-oxazolidone, 212 cc. of water, 8.9 g. of sulfuric acid and 30.1 g. of 5-nitro-2-furaldehyde diacetate[21] was steam distilled for 90 minutes. To the residue was added 50 cc. of isopropyl alcohol, the mixture refluxed for a few minutes and then cooled. The precipitate was removed by filtration, washed with water and isopropyl alcohol and dried to give 23.3 g., 93%, of N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone, m.p. 254–256°.

No reaction between methyl 5-nitro-2-furyl ketone or ethyl 5-nitro-2-furyl ketone with 3-amino-2-oxazolidone took place under the above conditions, but condensation was effected in either boiling 30% acetic acid or by heating the reactants in absolute alcohol with a little glacial acetic acid and a few crystals of iodine.

3-Amino-5-methyl-2-oxazolidone was condensed in acidic aqueous medium with 5-nitro-2-furaldehyde to give a quantitative yield of N-(5-nitro-2-furfurylidene)-3-amino-5-methyl-2-oxazolidone. The condensation of 5-nitro-2-furanacrolein with 3-amino-5-methyl-2-oxazolidone was carried out in boiling 30% acetic acid to give N-[(5-nitro-2-furyl)-acrylal]-3-amino-5-methyl-2-oxazolidone.

The 3-amino-4,5-dimethyl-2-oxazolidone oxalate reacted quantitatively in acidic aqueous medium with 5-nitro-2-furaldehyde to give N-(5-nitro-2-furfurylidene)-3-amino-4,5-dimethyl-2-oxazolidone. These new compounds are recorded in Table I.

Conversion of N-(5-Nitro-2-furfurylidene)-3-amino-5-hydroxymethyl-2-oxazolidone to N-(5-Nitro-2-furfurylidene)-3-amino-5-chloromethyl-2-oxazolidone.—To a mixture of 22 g. of N-(5-nitro-2-furfurylidene)-3-amino-5-hydroxymethyl-2-oxazolidone and 400 cc. of chloroform, was added 20 cc. of pyridine followed slowly by 62 cc. of thionyl chloride. The mixture was refluxed for 100 minutes (some foaming) and then allowed to remain at room temperature overnight. The reaction mixture was poured slowly into 2 liters of cold water and the solid removed by filtration. After washing with ethanol and ether, the N-(5-nitro-2-furfurylidene)-3-amino-5-chloromethyl-2-oxazolidone weighed 20 g., 85%, m.p. 196–197°. The melting point of a sample of material prepared by condensing 5-nitro-2-furaldehyde with 3-amino-5-chloromethyl-2-oxazolidone obtained by the method of Paterno and Cingolani[4] was 195–197°. A mixed melting point was not depressed and the ultraviolet absorption characteristics were identical.

NORWICH, N. Y.

(19) G. Gever and C. O'Keefe, U. S. Patent 2,660,607, Nov. 24, 1953 (*C. A.*, **48**, 12168b (1954)).

(20) T. Takahashi, *et al.*, *J. Pharm. Soc. Japan*, **69**, 284 (1949) (*C. A.*, **44**, 5372e (1950)).

(21) W. Kimel, J. Coleman and W. Stillman, U. S. Patent 2,490,006, Nov. 29, 1949 (*C. A.*, **44**, 1543g (1950)).