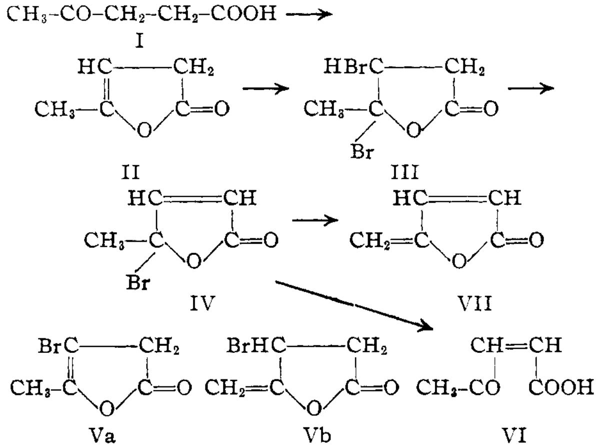


The yields depend to some extent on the tertiary base and the solvent, as indicated in Table I.

TABLE I

Solvent	Base	Protoanemonin, %[a,b]
Ether	Triethylamine	44
Ether	Pyridine	23
Ether	Picoline, techn.	73
Ether	2,4,6-Collidine	24
Ether	Quinoline	76
Benzene	Quinoline	99
Chloroform	Quinoline	12
Carbon disulfide	Quinoline	66

[a] Yields are based on α-angelica lactone. [b] A second distillation lowers the yield about 15% due to partial polymerization. The dimer, anemonin, can be isolated from the residue.

Replacement of the tertiary bases by calcium oxide or potassium hydroxide (in benzene) gave unsatisfactory results; in the latter case 11% of impure protoanemonin was obtained.

The dichlorovalerolactone, unlike the dibromide, is difficult to prepare, as addition of chlorine to the α-angelica lactone (II) always is accompanied by substitution. The dichlorolactone yielded with tertiary amines only an unsaturated monochlorolactone, probably analogous to IV, which could not be isolated in a pure state, but was characterized by its hydrolysis to β-acetylacrylic acid (VI). Our attempts to convert the monochlorolactone at higher temperatures to VII resulted in complete polymerization of the protoanemonin formed.

Experimental

Preparation of Protoanemonin (VII).—α-Angelica lactone (22.8), which was prepared by the slow dehydration of levulinic acid[3] in 90% yield, was dissolved in 25 ml. of carbon disulfide; 27.2 g. of bromine was added dropwise at about −20°. After the solution had become colorless, the carbon disulfide was evaporated under reduced pressure in a water-bath and the residue diluted with 200 ml. of the solvent; a trace of hydroquinone was added to prevent polymerization. Two equivalents of the tertiary amine was added dropwise at about −20°. After the mixture had stood overnight at room temperature, the precipitated hydrobromide of the amine was separated by filtration and washed thoroughly with the solvent. The solvent was removed from the combined filtrates under reduced pressure and the residue distilled at 12 mm. The fraction boiling between 65 and 80° was collected in a trap cooled with Dry Ice and acetone. A subsequent vacuum distillation immediately following the first yielded a pure product, b.p. 68° (8 mm.). The protoanemonin was identified as the crystalline dimer, anemonin, m.p. 153.5°.

Anal. Calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.17; double bonds, 2.00. Found: C, 61.66; H, 4.18; double bonds, 2.20.

Care is recommended in handling protoanemonin because of its vesicant properties. After the addition of a small amount of hydroquinone it can be stored unchanged in a refrigerator for several days. Without an inhibitor and at room temperature polymerization to anemonin begins very soon.

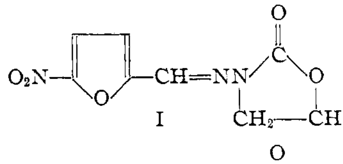
COLUMBUS 10, OHIO

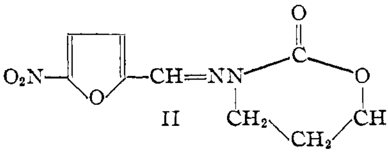
Chemotherapeutic Nitrofurans. III.[1] N-(5-Nitro-2-furfurylidene)-3-aminotetrahydro-1,3-oxazine-2-one

BY K. HAYES

RECEIVED OCTOBER 16, 1954

The chemotherapeutic effectiveness of N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone (I)[2,3] led to an interest in the preparation for microbiological testing of the six-membered ring analog, N-(5-nitro-2-furfurylidene)-3-aminotetrahydro-1,3-oxazine-2-one (II). This N-aminoheterocycle has not been prepared previously.


I


II

It was observed that 3-hydrazino-1-propanol[4] could be condensed and cyclized smoothly with diethyl carbonate in the presence of sodium methoxide to yield crude 3-aminotetrahydro-1,3-oxazine-2-one; when this was treated with 5-nitro-2-furaldehyde under acidic conditions it yielded II. The ultraviolet absorption characteristics of II are identical with those observed for the five-membered ring analog.[2]

Experimental

N-(5-Nitro-2-furfurylidene)-3-aminotetrahydro-1,3-oxazine-2-one.—A solution of 1.5 g. of sodium in 15 cc. of methanol was added to a mixture of 90 g. (1.0 mole) of 3-hydrazino-1-propanol and 150 g. (1.27 moles) of diethyl carbonate. The mixture was refluxed for two hours while the alcohol formed was removed continuously through a 20-inch Vigreux column. The oily residue was treated with 600 cc. of 3% hydrochloric acid and heated at 85° to hydrolyze the excess diethyl carbonate. A solution of 106 g. (0.75 mole) of 5-nitro-2-furaldehyde in 300 cc. of hot alcohol then was added. A yellow solid precipitated immediately. This was collected, after cooling, and washed by slurrying with two 200-cc. portions of alcohol and 200 cc. of ether; yield 110 g. (46%), m.p. 265–267°.

An analytical sample was prepared by recrystallizing twice from nitromethane and drying *in vacuo* at 56°. The material sublimes above 220° and melts at 267.5° (Fisher–Johns apparatus (cor.)); solubility in water 80 mg. per

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[1] For the previous paper in this series see THIS JOURNAL, **77**, 2282, (1955).

[2] For the first paper in this series see G. Gever, *et al.*, *ibid.*, **77**, 2277 (1955).

[3] J. Yurchenco, *et al.*, *Antibiotics and Chemotherapy*, **3**, 1035 (1953).

[4] G. Gever, THIS JOURNAL, **76**, 1283 (1954).

liter at 25°. Ultraviolet absorption E_{max} in 2% aqueous dimethylformamide 16500 at 366.0 mμ.

Anal. Calcd. for $C_9H_9N_3O_5$: C, 45.19; H, 3.79; N, 17.57. Found: C, 45.13; H, 3.80; N, 17.33.

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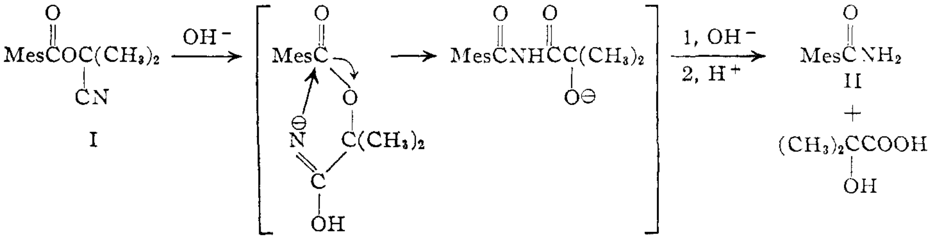
The Hydrolytic Rearrangement of α-Cyanoisopropyl Mesitoate[1]

BY JEREMIAH P. FREEMAN AND GEORGE B. LUCAS

RECEIVED DECEMBER 9, 1954

In connection with other work, the action of ethanolic sodium hydroxide on α-cyanoisopropyl mesitoate (I) has been examined. From this reaction, mesitamide (II) and α-hydroxyisobutyric acid were isolated. It is suggested that this reaction involves an intramolecular rearrangement which probably proceeds in the manner



Mes = 2,4,6-trimethylphenyl

Steric hindrance around the ester carbonyl group prevents attack of the hydroxide ion at that site so that the less reactive but unhindered nitrile function is attacked. Attack of the strongly nucleophilic intermediate imide ion on the carbonyl group is followed by tautomerization to the hydroxy imide which undergoes hydrolysis in the alkaline solution to mesitamide and α-hydroxyisobutyric acid. That the intramolecular rearrangement proceeds faster than simple hydrolysis of the nitrile is not unexpected since it has been demonstrated by Fuson and his co-workers[2,3] that the hindrance offered to intramolecular processes by the *o*-methyl groups is considerably less than to intermolecular processes. For instance, Fuson and Hammann[3] have shown that highly hindered ketones undergo a series of intramolecular ring closures involving the hindered carbonyl function and neighboring groups.

This hydrolytic rearrangement appears to be specific for sterically hindered esters as α-cyanoisopropyl benzoate was hydrolyzed rapidly and quantitatively to benzoic acid. In this case attack by hydroxide ion at the ester carbonyl proceeded normally.

Experimental[4]

α-Cyanoisopropyl Mesitoate.—To 51.0 g. (0.52 mole) of acetone cyanohydrin contained in a 200-ml. flask was added 91.5 g. (0.5 mole) of mesitoyl chloride with stirring. After addition was complete, the mixture was refluxed for two hours and then poured into water. The resulting mixture was extracted with four 100-ml. portions of methylene chloride. The organic extracts were washed with 10% sodium hydroxide solution and water, then dried and concentrated to yield 90.7 g. (79%) of α-cyanoisopropyl mesitoate, m.p. 40–42°. An analytical sample was prepared by distillation, b.p. 135–136° (8 mm.).

Anal. Calcd. for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 73.11; H, 7.63; N, 5.56.

Reaction of α-Cyanoisopropyl Mesitoate with Sodium Hydroxide.—A solution of 4.6 g. (0.02 mole) of α-cyanoisopropyl mesitoate in 50 ml. of ethanol was added to a solution of 8.0 g. (0.2 mole) of sodium hydroxide in 50 ml. of ethanol. The resulting mixture was heated under reflux for six hours and then poured into water. The solid that separated was collected on a filter; yield 1.6 g. The filtrate was extracted with ether and upon concentration of these extracts an additional 0.5 g. of solid was obtained. Recrystallization from benzene gave white crystals of mesitamide, m.p. 187–189° (lit. m.p.[5] 189°); total yield 2.1 g. (71%).

The aqueous extracts were acidified and subjected to continuous ether extraction for 18 hours. Upon drying and concentrating the ether solution there was obtained 1.8 g. (86%) of α-hydroxyisobutyric acid, which was identified by comparison of its infrared spectrum with that of an authentic sample.

α-Cyanoisopropyl Benzoate.—To 109.2 g. (0.52 mole) of trifluoroacetic anhydride contained in a 500-ml. 3-neck flask was added 62.2 g. (0.51 mole) of benzoic acid at 0–10°. The resulting mixture was stirred under reflux for 30 minutes. It was then cooled to 10° and 42.5 g. (9.5 mole) of acetone cyanohydrin was added at such a rate that the temperature did not rise above 20°. After the addition was complete the mixture was stirred at room temperature for 30 minutes, and then poured into water and the product isolated by conventional methods. α-Cyanoisopropyl benzoate was isolated by distillation at 0.01 mm. as a white solid, m.p. 37–38°, yield 48.7 g. (52%).

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86. Found: C, 69.51; H, 5.16.

Reaction of α-Cyanoisopropyl Benzoate with Sodium Hydroxide.—When 3.8 g. (0.02 mole) of α-cyanoisopropyl benzoate was treated with 8.0 g. of sodium hydroxide in the manner described for the corresponding mesitoate, 2.3 g. (96%) of benzoic acid, m.p. 120–122°, was obtained.

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[1] This work was carried out under Army Ordnance Contract W-01-021-ORD-334.

[2] R. C. Fuson, W. D. Emmons and R. Tull, *J. Org. Chem.*, **16**, 648 (1951).

[3] R. C. Fuson and W. C. Hammann, THIS JOURNAL, **74**, 1626 (1952).

[4] We are indebted to Dr. Keith S. McCallum for infrared interpretations and to Miss Annie Smelley for the micro-combustion data.

[5] I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1953, Vol. III, p. 84.

Perfluorinated Butadiene

BY A. L. HENNE AND WM. POSTELNECK

RECEIVED AUGUST 30, 1954

To allow a new, three-step synthesis of perfluorobutadiene,[1] we have treated 1,2,2-trifluoro-1,2-dichloroiodomethane[2,3] with zinc in acetic anhydride

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[1] W. T. Miller, *et al.*, *Ind. Eng. Chem.*, **39**, 401 (1947).

[2] J. T. Barr, *et al.*, THIS JOURNAL, **73**, 1352 (1951).

[3] R. N. Haszeldine, *J. Chem. Soc.*, 4423 (1952).