The product obtained on working up as usual melted at 156°. Mixed melting point with salicylic acid was not lowered.

4,4'-Methylenebis(3-hydroxycoumarin). A mixture of 3-hydroxycoumarin (1 g.), alcohol (20 ml.), and formalin (40% soln. 3 ml.) was refluxed for 3 hr. The separated product was filtered hot and crystallized from alcohol as colorless needles, m.p. 266°.

Anal. Calcd. for $C_{19}H_{12}O_6$: C, 67.85; H, 3.57. Found: C, 67.46; H, 3.35.

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The Mechanism of the Rearrangement of 2-Phenyl-4-hydroxymethylene-5-oxazolone[1,2]

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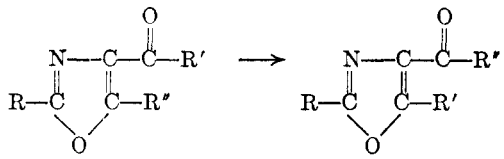
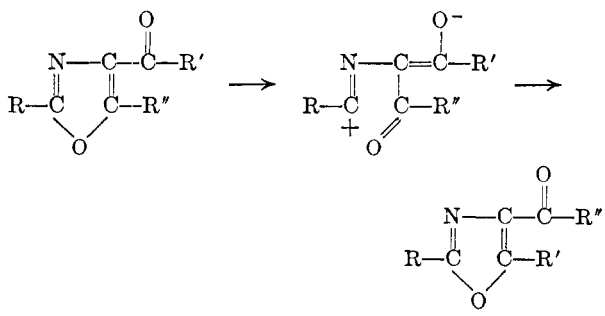
Synthetic work directed toward the synthesis of the erroneously postulated thiazolidine-oxazolone structure for penicillin led to a considerable advance in the chemistry of oxazolones. During the course of these studies a substance isomeric with 2-benzyl-4-hydroxymethylene-5-oxazolone was isolated from a reaction involving the latter compound. This isomeric compound was subsequently proved to be 2-benzyloxazole-4-carboxylic acid.[4a] Later several examples of the same general type of rearrangement came to light. The reaction can be formulated in general as an intramolecular rearrangement of 5-substituted oxazoles having a carbonyl carbon at C_4.[4b]



A direct interchange of R′ and R″ is rather unlikely. A more plausible mechanism, suggested by Cornforth,[4b] involves oxazole ring opening at C_2 followed by recyclization at the carbonyl oxygen.



We have substantiated this mechanism with C^{14} as a tracer.

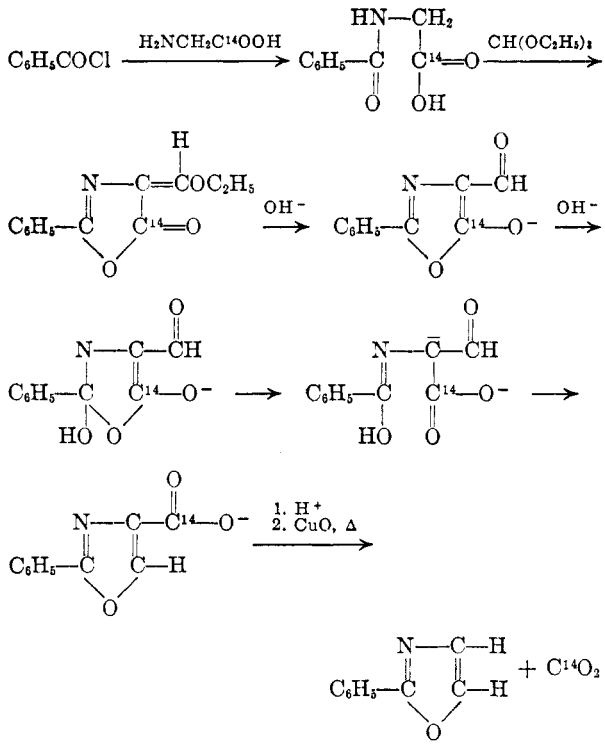


Table I shows that all of the radioactive carbon was in the carbon dioxide obtained by decarboxylation of the rearrangement product, 2-phenyloxazole-4-carboxylic acid.

TABLE I

COUNTING DATA FOR PERTINENT COMPOUNDS

Compound	Sample, Wt., Mg.	Count[a] per Min.	Background Count per Min.	Av. Count[b] per Min.
2-Phenyloxazole-4-carboxylic acid	106.2	2946	28	
	76.2	3024	28	2957
Barium carbonate	129.3	3166	30	
	122.1	3156	30	3131
2-Phenyloxazole	238.5	31	30	0

[a] After coincidence correction was applied. [b] All samples were of infinite thickness so that the total count is proportional to the specific activity.

Several attempts were made to prepare 2-phenyl-5-ethoxyoxazole-4-carboxylic acid from 2-phenyl-4-bromo-5-ethoxyoxazole *via* reaction with cuprous cyanide and with *n*-butyllithium. Neither reaction was successful under a wide variety of conditions.

(1) Abstracted from a Masters thesis by Dan Powers.

(2) Presented before the 134th meeting of the American Chemical Society, Chicago, Ill., Sept. 12, 1958.

(3) Present address: Department of Chemistry, Washington University, Seattle, Wash.

(4) H. T. Clarke, J. R. Johnson, and Sir Robert Robinson, *The Chemistry of Penicillin*, Princeton University Press, Princeton, N. J., 1949: (a) p. 694, (b) pp. 699–700, (c) p. 803.

EXPERIMENTAL

Hippuric-carboxyl-C^{14} acid. Glycine-1-C^{14} (3.48 mC./mM.; 0.5 mC. total activity; 10.8 mg.) was dissolved in water, and diluted to 10 ml. in a 10-ml. volumetric flask. Five cubic centimeters of this solution was pipeted into a solution prepared by dissolving 5.4 g. of inactive glycine and 12.5 g. of sodium hydroxide in 75 ml. of water. Benzoyl chloride (10 g.; 8.5 ml.) was then added and the mixture shaken vigorously until solution of the benzoyl chloride was complete. The solution was then acidified, filtered with suction, washed with water, and pressed as free of water as possible. The crude mixture was thoroughly mixed in the filter with two separate portions of ethyl ether and filtered. The yield of crude hippuric acid was 10 g. (78%).

2-Phenyl-4-ethoxymethylene-5-oxazolone-5-C^{14}. The 10 g. of hippuric acid obtained in the preceding preparation was mixed with 10 g. of inactive hippuric acid, added to a flask containing 12 ml. of acetic anhydride and 20 ml. of ethyl orthoformate and treated as previously described.[4c] The yield of oxazolone was 5 g. (22%).

2-Phenyloxazole-4-carboxylic-carboxyl-C^{14} acid. The hydrolysis and rearrangement of the oxazolone were carried out according to the procedure of Cornforth and Cookson.[5] The yield of a 2-phenyloxazole-4-carboxylic acid was 1.2 g. (67%).

Decarboxylation of 2-phenyloxazole-4-carboxylic-carboxyl-C^{14} acid. The acid was decarboxylated by distilling over copper-(II) oxide (bath temperature 270–280°). The carbon dioxide was absorbed in 0.2*N* barium hydroxide solution. The precipitated barium carbonate was isolated by filtration, washed successively with distilled water, acetone and ether, dried, and then counted.

The oxazole distillate was dissolved in ether and washed with aqueous sodium bicarbonate. The ether solution was dried, the ether evaporated, and the residual 2-phenyloxazole counted. The melting point of the picrate was 115–116° and was undepressed when mixed with an authentic specimen.

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(5) J. W. Cornforth and E. Cookson, *J. Chem. Soc.*, 1086 (1952).

The Free Radical Induced Rearrangement of 2-Methoxytetrahydropyran to Methyl Valerate

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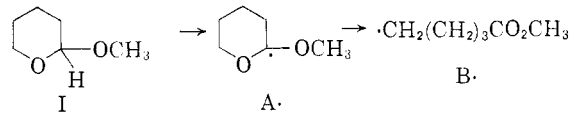
Acetals have been reported to react in a free radical chain reaction induced by alkoxy radicals yielding hydrocarbons and carbonyl-containing compounds as the main products.[2] The mechanism proposed to account for these products involves the abstraction of a hydrogen atom from the carbon atom adjacent to the oxygen producing a free radical, which undergoes decomposition into an alkyl radical and the carbonyl-containing compound.

$$R_2\dot{C}OR' \longrightarrow R_2C{=}O + R'\cdot$$

The investigation of 2-methoxytetrahydropyran (I) was undertaken to determine if this cyclic acetal could be rearranged to methyl valerate (II) *via* the following free radical chain sequence:



I A·

$$B\cdot + I \rightarrow CH_3(CH_2)_3CO_2CH_3 + A\cdot$$

II

The reaction of radical A· to form radical B· is the same type of elimination encountered in the reaction of Kuhn and Wellman. However, in the case of the cyclic radical A·, the elimination reaction amounts to a rearrangement of the radical.

Reactions in which di-*t*-butyl peroxide was thermally decomposed in the presence of 2-methoxytetrahydropyran have shown that rearrangement does in fact take place. Listed in Table I are the products obtained by heating 2-methoxytetrahydropyran with di-*t*-butyl peroxide at 120–130°.

TABLE I

PRODUCTS OBTAINED FROM THE DECOMPOSITION OF DI-*t*-BUTYL PEROXIDE IN 2-METHOXYTETRAHYDROPYRAN

	Moles	
	Run 1[a]	Run 2[b]
t-Butyl alcohol	0.21	0.18
Acetone	trace	trace
Methane	trace	trace
Methyl valerate	0.12	0.13
Residue	0.048 (m.w. 412)	(12.5 g.)
Recovered		
2-Methoxytetrahydropyran	0.08	0.25
Di-*t*-butyl peroxide	0.03	0.017

[a] 0.39 mole I, 0.15 mole di-*t*-butyl peroxide. [b] 0.48 mole I, 0.12 mole di-*t*-butyl peroxide.

The valerate ester was detected by the appearance of a strong ester carbonyl absorption at 5.76 μ in the infrared spectrum of the fraction collected at the boiling point of 2-methoxytetrahydropyran and methyl valerate (127°). The gas-liquid partition chromatographic analysis of this fraction showed the presence of two components with retention times corresponding to methyl valerate and 2-methoxytetrahydropyran. Chemical evidence of a valerate ester was obtained by preparation of the *p*-toluidide of valeric acid from the mixture. Conversion of the methyl ester to the *n*-butyl ester through an ester exchange reaction yielded *n*-butyl valerate which could be separated by distillation.

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(2) L. P. Kuhn and C. Wellman, *J. Org. Chem.*, 22, 774 (1956).