

2-OXAZOLIDONES

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I. INTRODUCTION AND NOMENCLATURE

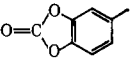
2-Oxazolidones (1), an important class of heterocyclic compounds containing a five-membered ring, have not been reviewed in detail. The related oxazolidines, which have a saturated five-membered ring containing nonadjacent oxygen and nitrogen atoms, have been reviewed (54), but their carbonyl-containing counterparts, the 2-oxazolidones, have not. Cornforth (104) has very briefly and incompletely covered the literature

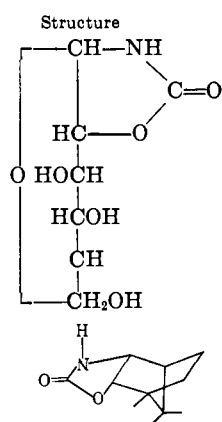
on 2-oxazolidones up to 1956, but his latest reported reference is 1953. Though no conscious effort has been made here to include Cornforth's material, much of it has crept in because of the necessity of organization.

The parent member of the series is variously referred to as 2-oxazolidone, 2-oxazolidinone, oxazolid-2-one, oxazolidin-2-one, oxazolidone-2, and oxazolidinone-2. The numbering system starts with the most electronegative element in the ring, oxygen, and assigns the next most electronegative element, nitrogen, the lowest

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TABLE I
 2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND PHOSGENE

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|----------------|------------------------------------|---|----------------|--|---------|---------------|
| C ₃ H ₅ NO ₂ | H | H | H | H | H | 89 | 60 | 464, 545 |
| C ₅ H ₇ NO ₄ | H | HOOC | H | Me | H | 196-197 dec (DL- <i>cis</i>) | 26 | 283, 285, 377 |
| C ₅ H ₉ NO ₃ | HOCH ₂ CH ₂ | H | H | H | H | 161 (0.1) | 50 | 544 |
| C ₆ H ₉ NO ₄ | EtOCO | H | H | H | H | 51-52 (EtOAc-heptane) | 95 | 50 |
| C ₆ H ₉ NO ₄ | CH ₂ =CHCH ₂ OCO | H | H | H | H | 41-42 (EtOAc-heptane) | 90 | 50 |
| C ₆ H ₁₁ NO ₄ | <i>n</i> -PrOCO | H | H | H | H | 53-54 (EtOAc-heptane) | 92 | 50 |
| C ₇ H ₁₁ NO ₂ | H | H | -(CH ₂) ₄ - | | H | <i>trans</i> , 99-100 (CHCl ₃ -pet. ether); 100-102; 100-110 (0.01) | 80 | 357, 358 |
| C ₈ H ₇ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | H | H | H | 255 | 62 | 205 |
| C ₈ H ₁₂ NO ₂ Cl | H | H | H | -(CH ₂) ₂ CH(CH ₂) ₂ - | | 150 | .. | 434 |
| C ₈ H ₁₃ NO ₂ | H | H | -(CH ₂) ₄ - | Me | H | <i>trans</i> , 107-109 (Et ₂ O-pet. ether) | 50 | 358 |
| C ₈ H ₉ NO ₂ | H | H | H | Ph | H | 87-87.5 (EtOH-hexane) | 96 | 426 |
| C ₁₀ H ₁₀ N ₂ O ₆ | <i>p</i> -O ₂ NC ₆ H ₄ CH ₂ | H | H | H | H | 171-173 (EtOAc-hexane) | 82 | 50 |
| C ₁₀ H ₁₁ NO ₂ | <i>m</i> -MeC ₆ H ₄ | H | H | H | H | .. | .. | 109 |
| C ₁₁ H ₁₁ NO ₄ | <i>p</i> -MeC ₆ H ₄ | H | H | H | H | .. | .. | 109 |
| C ₁₁ H ₁₁ NO ₄ | PhCH ₂ OCO | H | H | H | H | 101-102 (EtOAc-heptane) | 89 | 50 |
| C ₁₁ H ₁₂ NO ₄ Cl | H | H | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | H | 73.5 | .. | 12 |
| C ₁₁ H ₁₂ NO ₄ | H | H | H | <i>m</i> -ClC ₆ H ₄ OCH ₂ | H | 79-81 | .. | 12 |
| C ₁₁ H ₁₃ NO ₃ | H | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | H | 128-129 (EtOAc) | .. | 44 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 141-142 (H ₂ O) | 37 | 12, 322 |
| C ₁₂ H ₁₃ NO ₃ Cl ₂ | Et | H | H | <i>m</i> -MeOC ₆ H ₄ OCH ₂ | H | 121-123 | .. | 12 |
| C ₁₂ H ₁₄ NO ₃ Cl | Et | H | H | 2,4-Cl ₂ C ₆ H ₃ OCH ₂ | H | 215-220 (0.12) | 20 | 325 |
| C ₁₂ H ₁₄ NO ₃ Br | Et | H | H | <i>p</i> -ClC ₆ H ₄ OCH ₂ | H | 116-117 | 99 | 325 |
| C ₁₂ H ₁₅ NO ₃ | Et | H | H | <i>p</i> -BrC ₆ H ₄ OCH ₂ | H | 122.5 | 98 | 325 |
| C ₁₂ H ₁₅ NO ₄ | Me | H | H | PhOCH ₂ | H | 43-44 (<i>i</i> -Pr ₂ O), 182-185 (0.15) | 77 | 325 |
| | Me | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 77.5-78.5 (<i>i</i> -Pr ₂ O), 180-195 (0.08) | 73 | 12, 325 |
| | Me | H | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | .. | .. | 12 |
| | Me | H | H | <i>m</i> -MeOC ₆ H ₄ OCH ₂ | H | 73.5 | .. | 12 |
| | H | H | H | <i>o</i> -EtOC ₆ H ₄ OCH ₂ | H | 98-100 | .. | 12 |
| C ₁₃ H ₁₃ NO ₅ | <i>i</i> -Pr | H | H |  | H | 106-107 (C ₆ H ₆ -hexane) | .. | 520 |
| C ₁₃ H ₁₅ NO ₃ Cl | Et | H | H | 4-Cl-3-MeC ₆ H ₃ OCH ₂ | H | 94-94.5 (isooctane) | 82 | 325 |
| | Et | H | H | 3-Cl-2-MeC ₆ H ₃ OCH ₂ | H | 115-116 | 85 | 325 |
| | Et | H | H | 5-Cl-2-MeC ₆ H ₃ OCH ₂ | H | 77 (<i>i</i> -Pr ₂ O) | 45 | 325 |
| C ₁₃ H ₁₇ NO ₃ | Et | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | H | 50-50.5 (<i>i</i> -Pr ₂ O) | 59 | 325 |
| | Et | H | H | <i>m</i> -MeC ₆ H ₄ OCH ₂ | H | 50-51 | 40 | 325 |
| | Et | H | H | <i>p</i> -MeC ₆ H ₄ OCH ₂ | H | 90-91 (<i>i</i> -Pr ₂ O) | 52 | 325 |
| C ₁₃ H ₁₇ NO ₄ | Et | H | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | 80-81 (<i>i</i> -Pr ₂ O) | 96 | 325 |
| | Et | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 175-178 (0.1) | .. | 12 |
| C ₁₄ H ₁₉ NO ₃ | Et | H | H | 2,4-Me ₂ C ₆ H ₃ OCH ₂ | H | 37-38.5 (<i>i</i> -Pr ₂ O) | 56 | 325 |
| | Et | H | H | 3,5-Me ₂ C ₆ H ₃ OCH ₂ | H | 71-72 (<i>i</i> -Pr ₂ O), 204-205 (0.08) | .. | 325 |
| C ₁₄ H ₁₉ NO ₃ | <i>i</i> -Pr | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 76-78 (<i>i</i> -Pr ₂ O) | 28 | 325 |
| C ₁₅ H ₁₉ NO ₂ | H | Ph | H | Ph | H | <i>trans</i> , 159-160; <i>cis</i> , 188-189 | .. | 262 |
| C ₁₅ H ₂₁ NO ₂ | Et | H | H | 2,3,5-Me ₃ C ₆ H ₂ OCH ₂ | H | 154-155 (EtOAc) | 14 | 325 |
| C ₁₅ H ₂₁ NO ₄ | <i>n</i> -Bu | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 186-188 (0.03) | 76 | 325 |
| C ₁₆ H ₁₅ NO ₂ | Me | Ph | H | Ph | H | <i>trans</i> , 90; <i>cis</i> , 128 | .. | 262 |
| C ₁₆ H ₁₅ NO ₃ | Ph | H | H | PhOCH ₂ | H | 134.5-136.5 | 45 | 592 |
| C ₂₁ H ₁₇ NO ₂ | Ph | Ph | H | Ph | H | 216 (EtOH) | .. | 109 |
| C ₂₂ H ₁₉ NO ₂ | <i>m</i> -MeC ₆ H ₄ | Ph | H | Ph | H | 189 (EtOH) | .. | 109 |
| | <i>p</i> -MeC ₆ H ₄ | Ph | H | Ph | H | 209 (EtOH) | .. | 109 |

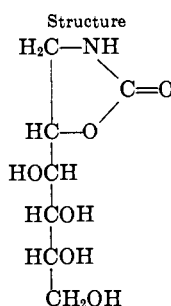


Mp, °C
220-222 dec (70%
aq MeOH)
tetraacetyl deriv,
150-151

Ref
501

123 (Et₂O)
(51% yield)

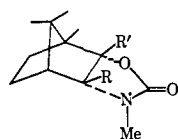
224



Mp, °C
155-156
tetraacetyl deriv,
126-127

Ref
501

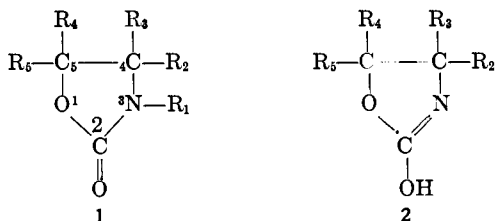
TABLE I (Continued)



Camphane Derivatives (224)

| R | R' | Mp or bp (mm), °C | % yield |
|-----|---------------------|----------------------------------|---------|
| H | Cl | 82 (Et ₂ O-hexane) | 70 |
| HO | H | 193 (MeOH-Et ₂ O) | 80 |
| HO | D | 192-193 | .. |
| H | H | 119 (Et ₂ O) | 60 |
| H | MeO | 122 | 60 |
| H | EtO | 145 (0.07) | 90 |
| H | AcO | 107 (hexane) | 87 |
| H | PhCH ₂ O | 153-154 | 87 |
| AcO | H | 120.5 (Et ₂ O) | 85 |
| Cl | Cl | 132 (Et ₂ O-hexane) | 80 |
| HO | Cl | 254 dec (MeOH-Et ₂ O) | 100 |
| AcO | Cl | 84-85 (Et ₂ O-hexane) | 65 |
| MeO | Cl | 76-78, 110-120 (0.05) | 60 |
| MeO | H | 48-50, 120-30 (0.15) | .. |

practical number. A tautomeric form can also be written when R₁ = H (2).



A standard designation for substituents on the parent oxazolidone ring has been adopted and used throughout, with a few clearly marked exceptions. In all preparative methods the nearest integral per cent yield is given as reported by the authors cited or as calculated from the data given wherever possible. Every effort has been expended to include all references to December 31, 1965, but, in such an active field as that of 2-oxazolidones, it is expected that there will be certain unavoidable omissions.

II. PREPARATION OF OXAZOLIDONES

A. INTRODUCTION

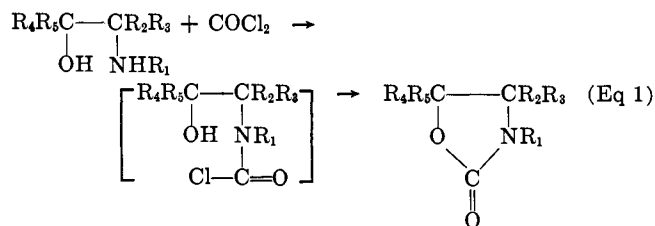
2-Oxazolidones can be looked upon as a two-carbon chain joined to a carbonyl group through oxygen on one side and nitrogen on the other. Since most classification systems are purely arbitrary, the view we have taken is that the carbon-carbon chain constitutes the "backbone" of the molecule, and classification of the numerous syntheses is made on this basis. In view of the numerous syntheses of 2-oxazolidones from compounds with vicinally substituted carbon atoms, such a classification is very convenient.

B. FROM β-AMINO ALCOHOLS

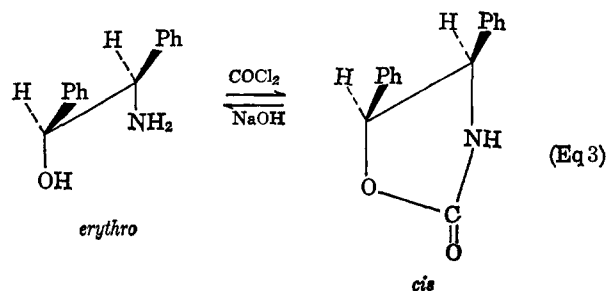
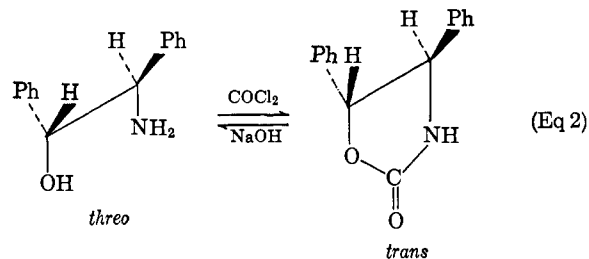
1. Using Phosgene (Table I)

One of the first reported and most general syntheses utilized a carbon-carbon chain with hydroxyl and

amino groups on adjacent carbon atoms (404). There must be at least one replaceable hydrogen atom in the amino group. The phosgene has been supplied as a gas (544, 545), in solution (50, 109, 283, 322, 520), or as a complex with pyridine (464), with and without added base (283, 501, 520) (Eq 1). The amino group would be expected to exhibit greater nucleophilicity than the hydroxyl, so that the first intermediate might be formulated as shown in Eq 1. One author (50), however, indicates primary reaction with the hydroxyl group when the amine is adjacent to a carbonyl group.



Studies have shown that the addition of phosgene does not alter the stereochemistry of the starting ma-

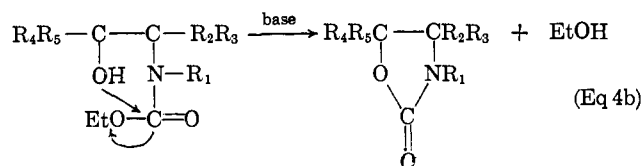
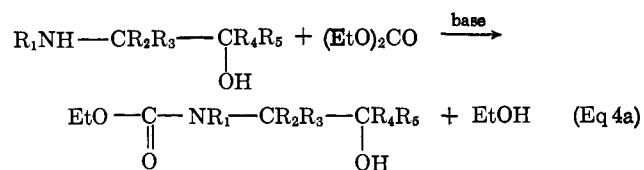


terial (262). Thus, *threo*- and *erythro*- β -amino alcohols give *trans*- and *cis*-4,5-disubstituted 2-oxazolidones, respectively, each of which can be hydrolyzed to afford the starting material (Eq 2 and 3).

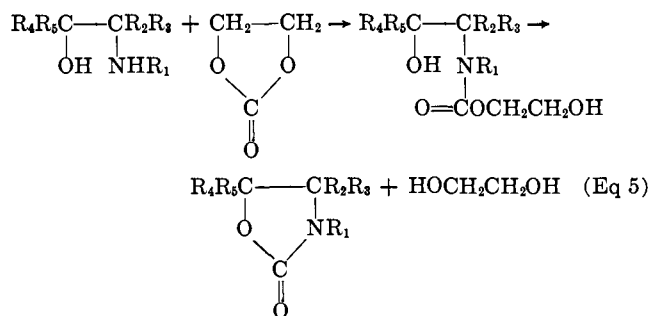
2. Using Dialkyl Carbonates (Table II)

Historically one of the earliest and certainly one of the key synthetic methods for the preparation of 2-oxazolidones is that of Homeyer (250). This is the reaction of diethyl carbonate with a β -amino alcohol catalyzed by basic substances, such as sodium methoxide, magnesium methoxide, potassium hydroxide, or sodium carbonate. The reaction has wide scope and synthetic utility.

Although the reaction might be looked upon as the generation of carbon dioxide *in situ* with its subsequent addition to the alcohol-amine system, accompanied by the elimination of the elements of water (*cf.* next section), the evidence suggests that the reaction proceeds in two stages (248): first, the more nucleophilic nitrogen displaces ethoxide giving ethyl alcohol plus the ethyl carbamate derivative (Eq 4a); second, cyclization takes place with elimination of another mole of ethyl alcohol (Eq 4b). Kinetic studies (526) have shown that the reaction is third order, first order in ethyl carbonate and second order in amino alcohol.

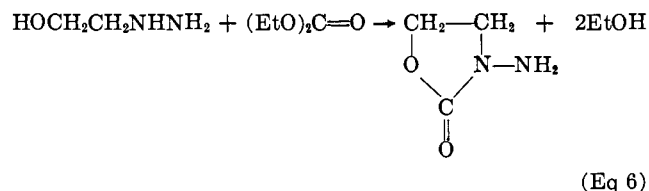


As a variant the cyclic carbonate, ethylene carbonate, has been used (74, 121, 147, 560) giving ethylene glycol in addition to the oxazolidone (Eq 5).



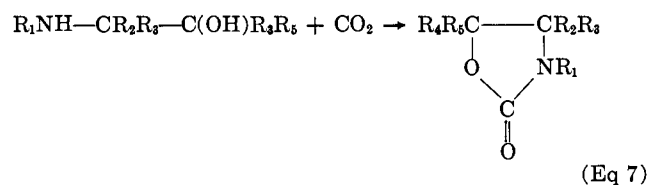
Although the R_1-N bond is usually a carbon-nitrogen bond, it may also be a nitrogen-nitrogen bond. The amino alcohol starting material is then a β -hydroxy-

hydrazine (197, 388, 423, 528, 529, 565) (Eq 6). The products are 3-amino-2-oxazolidones.



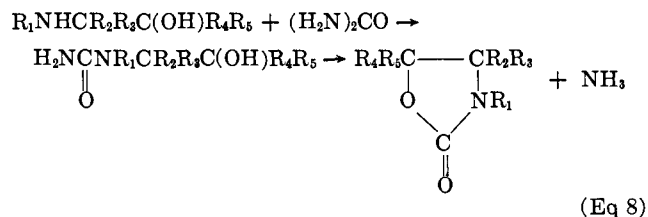
3. Using Carbon Dioxide (Table III)

Gaseous carbon dioxide has been used to produce 2-oxazolidones from β -amino alcohols in a limited number of cases described only in patents. The reactions are carried out with or without solvent at elevated temperatures under pressure (Eq 7). The reaction has the advantage of simplicity, but it has not been widely studied.



4. Using Urea (Table IV)

A more recent method for preparing 2-oxazolidones from β -amino alcohols utilizes urea as the other reactant. The reaction is carried out by fusion above the melting point of the reactants. It has been suggested (96, 97) that the urea first decomposes to form cyanic acid, which then reacts with the amino group to form a β -hydroxyethylurea derivative. This subsequently cyclizes with loss of ammonia to afford the product (Eq 8). The β -hydroxyethylurea can be synthesized separately by reaction of the amino group with an isocyanate. This product gives the 2-oxazolidone on heating (see next section).



It is reported that 2-oxazolidones are also obtained from β -amino alcohols and semicarbazones and even semicarbazide itself (514). In the cases reported the oxazolidones obtained were unsubstituted on nitrogen.

The formation of a 2-oxazolidone, or the failure to form one, has been used to determine the configuration of the ephedrine (96). The determination of configuration depends on whether the hydroxyl group is better situated for a displacement reaction or for con-

TABLE II
2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND DIALKYL CARBONATES

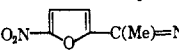

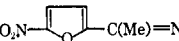
| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|--|---|---|----------------------------------|--|----------------|---|---------|--------------------|
| C ₃ H ₅ NO ₂ | H | H | H | H | H | 87-89 (CHCl ₃), 90-91 (ligroin), 170-172 (3) | 67 | 147, 250, 326, 560 |
| C ₃ H ₅ N ₂ O ₂ | H ₂ N | H | H | H | H | 69-71 (EtOH), 70.5-71 | 93 | 195, 389, 528 |
| C ₄ H ₈ NO ₂ Cl ₂ | H | H | H | Cl ₂ C | H | 125-125.5 (Me ₂ CO-EtOH) | ... | 74 |
| C ₄ H ₇ NO ₂ | H | H | H | Me | H | 111-113 (1) | ... | 48, 371 |
| | Me | H | H | H | H | 15, 87-90 (1) | ... | 48 |
| C ₄ H ₇ NO ₂ | H | H | H | HOCH ₂ | H | ... | ... | 13 |
| C ₄ H ₈ N ₂ O ₂ | H ₂ N | Me | H | H | H | ... | 36 | 205 |
| | H ₂ N | H | H | Me | H | 50.3-50.5 | 70 | 195, 205, 389 |
| C ₄ H ₈ N ₂ O ₂ | H ₂ N | HOCH ₂ | H | H | H | ... | 34 | 205 |
| | H ₂ N | H | H | HOCH ₂ | H | 156-157 | ... | 195, 227, 389 |
| C ₆ H ₇ NO ₂ Cl ₂ | H | ClCH ₂ | ClCH ₂ | H | H | ... | ... | 461 |
| C ₆ H ₈ NO ₂ Cl ₂ | ClCH ₂ CH ₂ | H | H | H | H | 137-138 (3) | ... | 121 |
| C ₆ H ₈ NO ₂ I | ICH ₂ CH ₂ | H | H | H | H | ... | ... | 121 |
| C ₆ H ₈ N ₂ O ₂ | CH ₃ CONH | H | H | H | H | 93-94 (EtOH) | 95 | 529 |
| C ₆ H ₈ NO ₂ | H | Me | Me | H | H | 55-56 (EtOH-pet. ether) | 86 | 156, 250, 382 |
| | Et | H | H | H | H | 95-95.5 (1.1), 92 (1), 78 (0.5) | ... | 250, 560 |
| | H | Et | H | H | H | 16-16.5 (CHCl ₃ -pet. ether) | 74 | 156, 250, 371, 382 |
| C ₆ H ₉ NO ₂ | HOCH ₂ CH ₂ | H | H | H | H | 164-166 (1) | ... | 48, 250 |
| | H | Me | HOCH ₂ | H | H | 115-116.5 (EtOH), 120 (EtOH-C ₆ H ₆) | 61 | 248, 250, 417 |
| C ₆ H ₉ NO ₄ | H | HOCH ₂ | HOCH ₂ | H | H | 109-110 (Me ₂ CO, then EtOH) | ... | 250 |
| C ₆ H ₁₀ N ₂ O ₂ | H ₂ N | Me | Me | H | H | 130-135 (10) | ... | 389 |
| | H ₂ N | Me | H | Me | H | ... | 45 | 195, 205, 389 |
| | H ₂ N | H | H | Et | H | ... | 20 | 205 |
| | H ₂ N | Et | H | H | H | ... | 62 | 205 |
| C ₆ H ₁₀ N ₂ O ₂ S | H ₂ N | H | H | MeSCH ₂ | H | ... | ... | 423 |
| C ₆ H ₉ NO ₄ | H | —OCMe ₂ O— | H | H | H | 164-165 (EtOAc) | 62 | 461 |
| C ₆ H ₁₀ NO ₂ Cl | Cl(CH ₂) ₃ | H | H | H | H | 156 (3) | ... | 121 |
| C ₆ H ₁₀ NO ₂ I | I(CH ₂) ₃ | H | H | H | H | ... | ... | 121 |
| C ₆ H ₁₀ N ₂ O ₂ | Me ₂ C=N | H | H | H | H | 110-115 (5) | ... | 565 |
| C ₆ H ₁₁ NO ₂ | H | Me | H | n-Pr | H | 133 (1.5) | ... | 250 |
| C ₆ H ₁₁ NO ₂ | H | H | H | HOCH ₂ | Et | ... | ... | 13 |
| C ₆ H ₁₂ N ₂ O ₂ | H ₂ N | n-Bu | H | H | H | 135 (0.7) | 46 | 195, 205, 389 |
| | H ₂ N | H | H | n-Bu | H | ... | 42 | 205 |
| C ₇ H ₁₃ NO ₂ | n-Bu | H | H | H | H | 98.2-99.3 (0.5), 94 (1) | ... | 147, 250 |
| C ₆ H ₇ N ₃ O ₂ | 5-Nitro-2-furfurylideneamino | H | H | H | H | 256-257 (DMF) | ... | 205, 274, 388, 523 |
| C ₆ H ₁₂ NO ₂ | H | —(CH ₂) ₄ — | H | H | H | 81-82 | 89 | 156, 382 |
| C ₆ H ₁₄ NO ₂ Cl | H | H | H | 2-Me-5-Cl-C ₆ H ₄ OCH ₂ | H | 77 | 45 | 319 |
| C ₆ H ₁₃ N ₂ O ₂ | H ₂ N | H | H | N-Pyrrolidinomethyl | H | 163-167 (2.5) | ... | 199 |
| C ₆ H ₁₃ N ₂ O ₂ | H ₂ N | H | H | N-Morpholinomethyl | H | 120 (i-PrOH) | ... | 200, 203, 227 |
| C ₆ H ₁₄ N ₂ O ₂ | H | H | H | Et ₂ NCH ₂ | H | 51.5-53 (EtOH) | 88.5 | 478 |
| C ₆ H ₁₇ N ₂ O ₂ I | Me ₃ N ⁺ CH ₂ CH ₂ I ⁻ | H | H | H | H | 227 | ... | 121 |
| C ₆ H ₁₇ N ₂ O ₂ | H ₂ N | H | H | Et ₂ NCH ₂ | H | 170-171, 138.5 (1.6) | ... | 200, 203 |
| C ₆ H ₈ N ₂ O ₂ Cl | 5-Nitro-2-furfurylideneamino | H | H | ClCH ₂ | H | 195-196 | ... | 205, 388 |
| C ₆ H ₉ NO ₂ | H | Ph | H | H | H | 136.8-137.8 | 92 | 156, 382 |
| | Ph | H | H | H | H | 118 (EtOH), 120-122.5 (CHCl ₃) | ... | 560, 598 |
| C ₆ H ₉ N ₂ O ₂ | 5-Nitro-2-furfurylideneamino | H | H | Me | H | 258-259, 255-256 | ... | 196, 205, 388 |
| | 5-Nitro-2-furfurylideneamino | Me | H | H | H | 199-200 | ... | 196, 205, 388 |
| |  | H | H | H | H | 133 | ... | 205 |
| C ₆ H ₉ N ₃ O ₂ | 5-Nitro-2-furfurylideneamino | H | H | HOCH ₂ | H | 241-243 | ... | 205, 388 |
| C ₆ H ₁₂ NO ₄ | H |  | H | H | H | 201-202 (Me ₂ CO) | ... | 461 |
| C ₆ H ₁₂ NO ₂ | Cyclohexyl | H | H | H | H | 33-34, 151-153 (4), 128-131 (0.5-1.0) | ... | 560, 598 |
| C ₆ H ₁₇ N ₂ O ₂ | H ₂ N | H | H | N-Piperidinomethyl | H | 128-129 | 44 | 200, 203 |
| C ₆ H ₁₈ N ₂ O ₂ | H | HOCH ₂ | Et ₂ NCH ₂ | H | H | 51-54 (pentane), 205-210 (0.08) | 54 | 461 |
| C ₆ H ₁₉ N ₂ O ₂ I | Me ₃ N ⁺ (CH ₂) ₃ I ⁻ | H | H | H | H | 123 | ... | 121 |
| C ₁₀ H ₈ NO ₂ Cl ₂ | H | H | H | 2,4,6-Cl ₃ C ₆ H ₂ OCH ₂ | H | ... | ... | 319 |
| C ₁₀ H ₈ N ₂ O ₂ Cl ₂ | H | H | H | 2,4-Cl ₂ C ₆ H ₃ OCH ₂ | H | 128-130 | ... | 319 |
| C ₁₀ H ₁₁ NO ₂ | H | Me | Ph | H | H | 79.6-80.0 | 82 | 156, 382 |
| | H | Me | H | Ph | H | 145-146 | ... | 250 |
| C ₁₀ H ₁₁ N ₂ O ₂ | 5-Nitro-2-furfurylideneamino | Me | Me | H | H | 152-153 | ... | 205, 388 |
| | 5-Nitro-2-furfurylideneamino | Me | H | Me | H | 143-144 | ... | 205, 388 |
| | 5-Nitro-2-furfurylideneamino | H | H | Et | H | 215-216 | ... | 205, 388 |
| | 5-Nitro-2-furfurylideneamino | Et | H | H | H | 142-143 | ... | 205 |
| |  | H | H | Me | H | 120-122 | ... | 205 |

TABLE II (Continued)

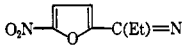
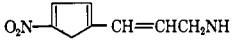
| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|--------------------|----------------|---|----------------|---|---------|----------|
| |  | H | H | H | H | 102 | ... | 205 |
| |  | H | H | H | H | 132-135 | ... | 388 |
| C ₁₀ H ₁₁ N ₂ O ₃ S | 5-Nitro-2-furfurylideneamino | H | H | MeSCH ₂ | H | 182 (HOAc) | ... | 423 |
| C ₁₀ H ₁₁ N ₂ O ₇ S | 5-Nitro-2-furfurylideneamino | H | H | MeSO ₂ CH ₂ | H | 195 | ... | 423 |
| C ₁₀ H ₁₃ NO ₄ | H | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 140.5-142.0 (EtOH) | ... | 323 |
| C ₁₀ H ₁₂ N ₂ O ₃ Cl | H | H | H | 2-Pr-6-ClC ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₀ H ₁₂ N ₂ O ₄ Cl | H | H | H | 2-PrO-6-ClC ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₀ H ₁₇ NO ₂ | PhCH ₂ | H | H | H | H | 78-80 (pet. ether-C ₆ H ₆) | 91 | 598 |
| C ₁₁ H ₁₁ N ₂ O ₃ F | H | H | H | 2-Me-4-FC ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₁ H ₁₁ N ₂ O ₃ Br | H | H | H | 2-Me-4-BrC ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₁ H ₁₁ N ₂ O ₂ Cl | PhCH=N | H | H | ClCH ₂ | H | 117.5-118 (abs. EtOH) | ... | 227 |
| C ₁₁ H ₁₁ N ₂ O ₃ S | 5-Nitro-2-furfurylideneamino | H | H | CH ₂ =CHSCH ₂ | H | 150 | ... | 423 |
| C ₁₁ H ₁₂ N ₂ O ₂ | PhCH=N | H | H | HOCH ₂ | H | 138-138.5 (abs. EtOH) | ... | 227 |
| C ₁₁ H ₁₂ NO ₂ | Me | Me | H | Ph | H | 92-92.5 (C ₆ H ₆ -pet. ether) | 89 | 250 |
| C ₁₁ H ₁₂ N ₂ O ₇ S | 5-Nitro-2-furfurylideneamino | H | H | EtSO ₂ CH ₂ | H | 159 | ... | 423 |
| C ₁₁ H ₁₂ N ₂ O ₂ | H ₂ N | H | H | PhMeNCH ₂ | H | 214-215 | ... | 200 |
| C ₁₁ H ₁₂ N ₂ O ₃ Cl | Pr | H | H | 2-Me-3-ClC ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₁ H ₁₂ N ₂ O ₃ | Me ₂ C=N | H | H | N-Morpholinomethyl | H | 172-175 (1-2) | 75 | 567 |
| C ₁₁ H ₁₂ N ₂ O ₂ I | Et ₂ N ⁺ CH ₂ CH ₂ I ⁻ | H | H | H | H | 116 | ... | 121 |
| C ₁₂ H ₁₂ N ₂ O ₂ Cl ₂ | Et | H | H | 2,4-Cl ₂ C ₆ H ₃ OCH ₂ | H | 215-220 (0.12) | 20 | 325 |
| C ₁₂ H ₁₂ N ₂ O ₃ S | 5-Nitro-2-furfurylideneamino | H | H | CH ₂ =CHCH ₂ SCH ₂ | H | 118 | ... | 423 |
| C ₁₂ H ₁₂ N ₂ O ₃ | H | H | H | 2,6-Me ₂ C ₆ H ₃ OCH ₂ | H | 117.0-118.5 | ... | 319 |
| | Et | H | H | PhOCH ₂ | H | 43-44 (<i>i</i> -Pr ₂ O), 182-185 (0.15) | 77 | 325 |
| C ₁₂ H ₁₂ N ₂ O ₃ Cl | Et | H | H | <i>p</i> -ClC ₆ H ₄ OCH ₂ | H | 116-117 | 99 | 325 |
| C ₁₂ H ₁₂ N ₂ O ₃ Br | Et | H | H | <i>p</i> -BrC ₆ H ₄ OCH ₂ | H | 122.5 | 98 | 325 |
| C ₁₂ H ₁₂ N ₂ O ₄ | Me | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 77.5-78.5 (<i>i</i> -Pr ₂ O), 73-75, 180-195 (0.08) | 73 | 321 |
| C ₁₂ H ₁₂ N ₂ O ₅ | H | H | H | 2,6-(MeO) ₂ C ₆ H ₃ OCH ₂ | H | 104-105, 117-118.5 | ... | 319, 321 |
| C ₁₂ H ₁₂ N ₂ O ₃ | 5-Nitro-2-furfurylideneamino | Bu | H | H | H | 150-151 | ... | 205, 388 |
| | 5-Nitro-2-furfurylideneamino | H | H | Bu | H | 194 | ... | 205, 388 |
| C ₁₂ H ₁₂ N ₂ O ₃ S | 5-Nitro-2-furfurylideneamino | H | H | <i>n</i> -PrSCH ₂ | H | 148 | ... | 423 |
| | 5-Nitro-2-furfurylideneamino | H | H | <i>i</i> -PrSCH ₂ | H | 170 | ... | 423 |
| C ₁₂ H ₁₂ N ₂ O ₇ S | 5-Nitro-2-furfurylideneamino | H | H | <i>n</i> -PrSO ₂ CH ₂ | H | 158 | ... | 423 |
| | 5-Nitro-2-furfurylideneamino | H | H | <i>i</i> -PrSO ₂ CH ₂ | H | 180 | ... | 423 |
| C ₁₂ H ₁₂ N ₂ O ₂ I | Et ₂ N ⁺ (CH ₂) ₃ I ⁻ | H | H | H | H | 131 | ... | 121 |
| C ₁₂ H ₁₂ N ₂ O ₂ | H ₂ N | H | H | Bu ₂ NCH ₂ | H | 152.5-153.5 | ... | 200 |
| C ₁₃ H ₁₂ N ₂ O ₃ Cl | Et | H | H | 3-Cl-2-MeC ₆ H ₃ OCH ₂ | H | 110-111, 115-116 | 85 | 319, 325 |
| | Et | H | H | 4-Cl-3-MeC ₆ H ₃ OCH ₂ | H | 94-94.5 (isooctane) | 82 | 325 |
| | Et | H | H | 5-Cl-2-MeC ₆ H ₃ OCH ₂ | H | 77 (<i>i</i> -Pr ₂ O) | 45 | 325 |
| C ₁₃ H ₁₂ N ₂ O ₃ | 5-Nitro-2-furfurylideneamino | H | H | N-Morpholinomethyl | H | 169.5-170.5 (EtOH) (<i>n</i> form) 208-209 (<i>i</i> -PrOH-MeNO ₂) (<i>l</i> form) | ... | 227 |
| C ₁₃ H ₁₇ NO ₃ | Et | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | H | 50-50.5 (<i>i</i> -Pr ₂ O) | 59 | 325 |
| | Et | H | H | <i>m</i> -MeC ₆ H ₄ OCH ₂ | H | 50-51 | 40 | 325 |
| | Et | H | H | <i>p</i> -MeC ₆ H ₄ OCH ₂ | H | 90-91 (<i>i</i> -Pr ₂ O) | 52 | 325 |
| C ₁₃ H ₁₇ NO ₄ | Et | H | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | 80-81 (<i>i</i> -Pr ₂ O) | 96 | 325 |
| C ₁₃ H ₁₇ N ₂ O ₂ | Et | H | H | <i>p</i> -MeC ₆ H ₄ NHCH ₂ | H | 67-68 (ligroin-C ₆ H ₆) | 91 | 314 |
| C ₁₃ H ₁₇ N ₂ O ₃ S | 5-Nitro-2-furfurylideneamino | H | H | <i>n</i> -BuSCH ₂ | H | 134 | ... | 423 |
| C ₁₃ H ₁₇ N ₂ O ₇ S | 5-Nitro-2-furfurylideneamino | H | H | <i>n</i> -BuSO ₂ CH ₂ | H | 150 | ... | 423 |
| C ₁₄ H ₁₂ NO ₃ | H | H | H | 2,6-Et ₂ C ₆ H ₃ OCH ₂ | H | ... | ... | 319 |
| C ₁₄ H ₁₂ N ₂ O ₃ | <i>p</i> -MeC ₆ H ₄ | H | H | N-Morpholinyl | H | 119.5-120.5 (ligroin-C ₆ H ₆) | 96 | 314 |
| C ₁₄ H ₁₂ N ₄ O ₃ | 5-Nitro-4-furfurylideneamino | H | H | N-Piperidinomethyl | H | 197-198 (EtOH) | ... | 200 |
| C ₁₄ H ₁₂ N ₄ O ₃ | 5-Nitro-4-furfurylideneamino | H | H | 2-Me-N-morpholinomethyl | H | 174 | ... | 168 |
| C ₁₄ H ₁₂ NO ₃ | Et | H | H | 2,4-Me ₂ C ₆ H ₃ OCH ₂ | H | 37-38.5 (<i>i</i> -Pr ₂ O) | 56 | 325 |
| | Et | H | H | 3,5-Me ₂ C ₆ H ₃ OCH ₂ | H | 71-72 (<i>i</i> -Pr ₂ O), 202-205 (0.08) | 42 | 325, 437 |
| C ₁₄ H ₁₂ NO ₄ | <i>i</i> -Pr | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 76-78 (<i>i</i> -Pr ₂ O) | 28 | 325 |
| C ₁₄ H ₁₂ N ₂ O ₂ Cl | <i>n</i> -Bu | H | H | <i>p</i> -ClC ₆ H ₄ NHCH ₂ | H | 81.5-82.5 (ligroin-C ₆ H ₆) | 78 | 314 |
| C ₁₄ H ₂₀ N ₂ O ₂ | <i>n</i> -Pr | H | H | <i>p</i> -MeC ₆ H ₄ NHCH ₂ | H | 94-96 (ligroin-C ₆ H ₆) | 90 | 314 |
| | <i>n</i> -Bu | H | H | PhNHCH ₂ | H | 74-76 (Et ₂ O) | 86 | 314 |
| C ₁₄ H ₂₁ N ₂ O ₂ I | (PhCH ₂)Me ₂ N ⁺ CH ₂ CH ₂ I ⁻ | H | H | H | H | 170 | ... | 121 |
| C ₁₅ H ₁₂ NO ₂ | H | H | H | Ph | Ph | ... | ... | 382 |
| | H | Ph | Ph | H | H | 178.4-178.8 | 98 | 156, 382 |
| C ₁₅ H ₁₂ N ₂ O ₂ | H | N-Piperidinomethyl | H | H | H | 180-181 (EtOH) | ... | 461 |
| C ₁₅ H ₁₂ N ₄ O ₃ | 5-Nitro-2-furfurylideneamino | H | H | (CH ₂ =CHCH ₂) ₂ NCH ₂ | H | 151 | ... | 168 |
| C ₁₅ H ₁₂ N ₄ O ₃ | PhCH=N | H | H | N-Morpholinomethyl | H | 169.5-170.5 (EtOH) | ... | 227 |
| C ₁₅ H ₂₀ N ₄ O ₃ | 5-Nitro-2-furfurylideneamino | H | H | 2,6-Me ₂ -N-morpholinomethyl | H | 203 | ... | 168 |
| C ₁₅ H ₂₀ N ₅ O ₃ | 5-Nitro-2-furfurylideneamino | H | H | N-Me-N'-piperazinomethyl | H | 197 | ... | 168 |
| C ₁₅ H ₂₁ NO ₃ | Et | H | H | 2,3,5-Me ₃ C ₆ H ₂ OCH ₂ | H | 154-155 (EtOAc) | 14 | 325 |
| C ₁₅ H ₂₁ NO ₄ | <i>n</i> -Bu | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 186-188 (0.03) | 76 | 325 |
| C ₁₅ H ₂₂ N ₂ O ₂ | <i>n</i> -Bu | H | H | <i>p</i> -MeC ₆ H ₄ NHCH ₂ | H | 73.5-74.5 (ligroin-C ₆ H ₆) | 96 | 314 |
| | <i>n</i> -Bu | H | H | <i>m</i> -MeC ₆ H ₄ NHCH ₂ | H | 55.5-56.5 (ligroin-C ₆ H ₆) | 94 | 314 |

TABLE II (Continued)

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|----------------|----------------|--|----------------|--|---------|----------|
| C ₁₆ H ₂₂ N ₂ O ₆ | 5-Nitro-2-furfurylideneamino | H | H | N-Et-N'-piperazino-methyl | H | 193 | ... | 168 |
| | 5-Nitro-2-furfurylideneamino | H | H | 3,4-Me ₂ -N-piperazino-methyl | H | 161-164 | ... | 168 |
| | 5-Nitro-2-furfurylideneamino | H | H | 2,4-Me ₂ -N-piperazino-methyl | H | 191-193 | ... | 168 |
| C ₁₆ H ₂₂ NO ₄ | H | H | H | 2,6-(<i>n</i> -PrO) ₂ C ₆ H ₃ OCH ₂ | H | ... | ... | 319, 321 |
| C ₁₆ H ₂₂ N ₂ O ₂ | <i>n</i> -Am | H | H | <i>p</i> -MeC ₆ H ₄ NHCH ₂ | H | 81-82 (ligroin-C ₆ H ₆) | 92 | 314 |
| C ₁₆ H ₂₄ N ₂ O ₂ | Ph | H | H | <i>n</i> -Bu ₂ NCH ₂ | H | 32-33 (Et ₂ O-pet. ether) | 87 | 314 |
| C ₁₇ H ₂₂ NO ₄ | Cyclohexyl | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 68-69 | ... | 321 |
| C ₁₇ H ₂₂ N ₂ O ₅ | 5-Nitro-2-furfurylideneamino | H | H | N- <i>n</i> -Pr-N'-piperazino-methyl | H | 184-185 | ... | 168 |
| C ₁₈ H ₁₉ NO ₄ | PhCH ₂ | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 59-59.5 (isooctane-Et ₂ O) | 70 | 321, 325 |
| C ₁₈ H ₂₀ N ₂ O ₂ | <i>p</i> -MeC ₆ H ₄ | H | H | <i>p</i> -MeC ₆ H ₄ NHCH ₂ | H | 157-158.5 (ligroin-C ₆ H ₆) | 87 | 314 |
| C ₁₈ H ₂₁ N ₂ O ₂ | H ₂ N | H | H | (PhCH ₂) ₂ NCH ₂ | H | 163-165 | ... | 200-203 |
| C ₂₀ H ₂₄ N ₂ O ₂ | Ph | H | H | <i>n</i> -BuPhNCH ₂ | H | 214-216 (1.5) | 64 | 314 |
| | | | | | | 106-108 (EtOH) | ... | 250 |

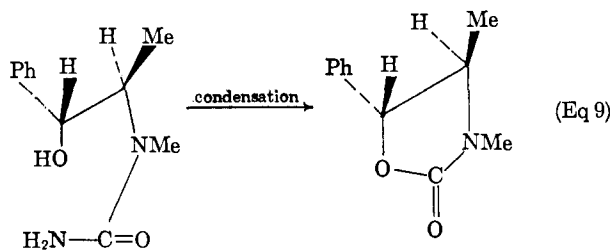
TABLE III

2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND CARBON DIOXIDE

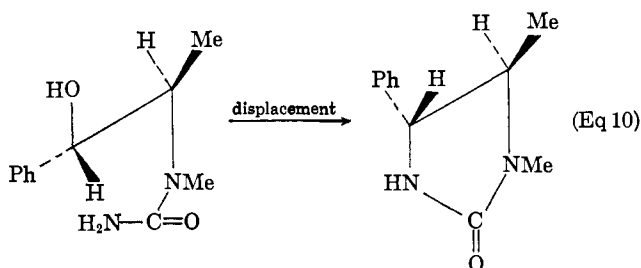
| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|---------------------------------------|----------------|----------------------------|---------|-----|
| C ₃ H ₉ NO ₂ | H | H | 88-89 (CHCl ₃) | 35 | 326 |
| C ₅ H ₉ NO ₂ | Me | Me | 92 (1.5) | 58 | 495 |
| C ₆ H ₁₁ NO ₂ | Et | Me | 87 (1) | .. | 495 |
| C ₇ H ₁₃ NO ₂ | CH ₃ CH(OH)CH ₂ | Me | 132-133 (0.2) | 76 | 495 |
| C ₈ H ₁₅ NO ₂ | Et | <i>i</i> -Pr | 107 (1) | .. | 495 |

^a R₂ = R₃ = R₅ = H.

densation with elimination of water after fusion with urea (Eq 9 and 10).



from (+)-pseudoephedrine

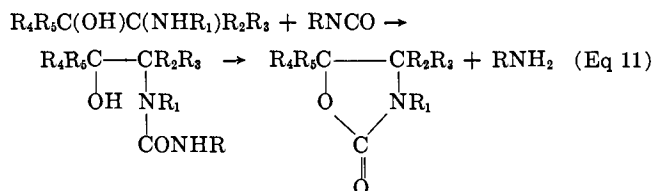


from (-)-ephedrine

One worker (425) claims to have produced 2-oxazolidone itself by first forming the β -hydroxyethylurea, nitrosating, and then cyclizing.

5. Use of Isocyanates (Table V)

Urea derivatives are obtained by reaction of β -amino alcohols with organic isocyanates (588) or inorganic cyanates (205, 261). The substituted urea is then cyclized by heating alone (588) or by heating in the presence of urea (261) or with hydrochloric acid (262). Ammonia or an amine is eliminated (Eq 11).



6. Use of Ethyl Chlorocarbonate (Chloroformate) (Table VI)

Ethyl chlorocarbonate in the presence of bases, such as sodium hydroxide, sodium ethoxide, sodium acetate, and potassium carbonate, has been used to a moderate extent to convert β -amino alcohols to 2-oxazolidones. Evidence (166) points to primary reaction with the amino group, with elimination of HCl, to form the N-carbonyloxy derivative (β -hydroxyurethan). This subsequently cyclizes with loss of ethanol (Eq 12).

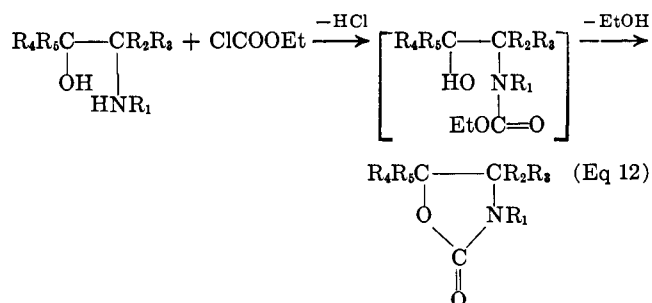
TABLE IV
 2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND UREAS

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|-----------------------------------|-------------------|------------------------------------|----------------|----------------|--|---------|--------------|
| C ₃ H ₅ NO ₂ | H | H | H | H | H | 85-87 (CHCl ₃) | 83 | 251 |
| C ₄ H ₇ NO ₂ | Me | H | H | H | H | 180 (1.5) | ... | 251 |
| | | H | H | Me | H | 20-22, 110-111 (0.1-0.2) | ... | 57, 251, 481 |
| C ₅ H ₉ NO ₂ | H | Me | Me | H | H | 56.5-58 (EtOH-Et ₂ O) | 13 | 97 |
| | H | H | H | Me | Me | 79-82 (EtOH-Skellysolve B) | 53 | 97 |
| C ₆ H ₉ NO ₃ | H | HOCH ₂ | Me | H | H | 115 (MeOH, then Me ₂ CO) | 73 | 251 |
| C ₆ H ₉ NO ₄ | H | HOCH ₂ | HOCH ₂ | H | H | 107-109 (EtOH) | 69 | 251 |
| C ₇ H ₁₁ NO ₂ | H | H | -(CH ₂) ₄ - | H | H | <i>trans</i> , 100-102 (CHCl ₃ -pet. ether) | 10 | 357, 358 |
| C ₈ H ₇ N ₃ O ₆ | 5-Nitro-2-furfuryl- ideneamino | H | H | H | H | 253-255 | ... | 101, 424 |
| C ₁₀ H ₁₁ NO ₂ | H | Me | H | Ph | H | 123 | ... | 514, 515 |
| C ₁₁ H ₁₃ NO ₂ | Me | Me | H | Ph | H | ... | ... | 96 |
| | H | H | H | Ph | Et | 119-120 (EtOH-Skellysolve B) | 83 | 97 |
| C ₁₃ H ₁₇ NO ₂ | H | H | H | <i>i</i> -Bu | Me | 69-70 (EtOH-Skellysolve B) | 60 | 97 |
| | H | Me | Me | <i>i</i> -Pr | H | 50-52 (Et ₂ O-Skellysolve B) | 83 | 97 |
| C ₁₄ H ₁₃ NO ₂ | H | Ph | H | Ph | H | <i>trans</i> , 159-160; <i>cis</i> , 188-190 | 73 (†) | 261 |
| | H | H | H | Ph | Ph | 199-200 (EtOH) | 82 | 97 |
| C ₁₆ H ₁₅ NO ₂ | Me | Ph | H | Ph | H | <i>trans</i> , 90 | ... | 261 |

 TABLE V
 2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND ORGANIC ISOCYANATES OR INORGANIC CYANATES

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|----------------|------------------------------------|--|---|---------|----------|
| C ₂ H ₅ NO ₂ | H | H | H | 90 (EtOH) | .. | 290 |
| C ₆ H ₁₁ NO ₂ | H | Me | Et | 143-144 (2) | 53 | 588 |
| C ₇ H ₁₁ NO ₂ | H | -(CH ₂) ₄ - | | <i>trans</i> , 100-102; <i>cis</i> , 55-56 | .. | 357 |
| C ₈ H ₁₃ NO ₂ | Me | -(CH ₂) ₄ - | | <i>trans</i> , 51-52; <i>cis</i> , liquid | .. | 357 |
| C ₁₀ H ₁₀ NO ₂ Cl | H | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | 151 (EtOAc) | .. | 44 |
| C ₁₆ H ₁₃ NO ₂ | H | Ph | Ph | <i>cis</i> , 188-190 | 62 | 261, 262 |
| C ₁₆ H ₁₅ NO ₂ | Me | Ph | Ph | <i>trans</i> , 90 | .. | 261, 262 |

^a R₃ = R₅ = H.



Stereochemical studies have not been reported other than that the ephedrines yield different oxazolidones (166).

7. Use of Esters of Trichloroacetic Acid (Table VII)

One of the new methods for synthesizing 2-oxazolidones uses methyl or ethyl trichloroacetate as the cyclizing reagents for β -amino alcohols without the use

of added catalysts or elevated temperatures. One proposed mechanism (305, 306) suggests primary attack (alcoholysis) by the alcohol function of the amino alcohol on the ester with displacement of methyl or ethyl alcohol, then cyclization by internal nucleophilic attack by nitrogen on the carbonyl carbon followed by elimination of chloroform (Eq 13).

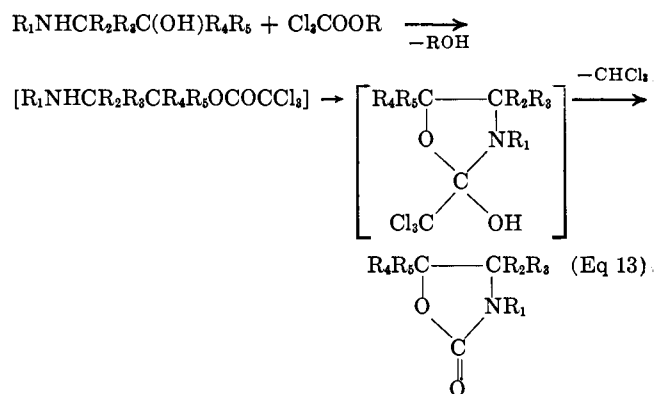


TABLE VI
 2-OXAZOLIDENES PREPARED FROM β -AMINO ALCOHOLS AND ETHYL CHLOROCARBONATE (CHLOROFORMATE)

| Empirical formula ^a | R ₁ | R ₂ | R ₃ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|--|----------------------------------|---|---------------------|--|---------|----------|
| C ₈ H ₆ NO ₂ | H | H | H | H | 87 | 60 | 562 |
| C ₆ H ₇ N ₃ O ₈ | H | O ₂ NOCH ₂ | O ₂ NOCH ₂ | H | 106-107 | .. | 60 |
| C ₅ H ₉ NO ₄ | H | HOCH ₂ | HOCH ₂ | H | 109.5-110.7 (MeOH) | 68 | 60, 90 |
| C ₆ H ₁₁ NO ₂ | H | H | H | <i>i</i> -Pr | (D) 113-114 (C ₆ H ₆ -ligroin, then C ₆ H ₆) | .. | 376 |
| C ₈ H ₇ N ₃ O ₅ | 2-Furfurylideneamino | H | H | H | 173-174 (50% EtOH) | 90 | 444 |
| C ₉ H ₁₃ NO ₆ | H | MeCOOCH ₂ | MeCOOCH ₂ | H | 69-70.4 | .. | 90 |
| C ₉ H ₁₇ NO ₃ | <i>i</i> -Bu | Me | HOCH ₂ | H | 72-73, 121-122 (0.01) | 53 | 351 |
| C ₁₀ H ₁₀ N ₂ O ₂ | PhCH=N | H | H | H | 143-145 (EtOH) | 85 | 141, 205 |
| C ₁₀ H ₁₀ N ₃ O ₄ | <i>p</i> -O ₂ NC ₆ H ₄ CH=N | H | H | H | 227-229 | .. | 444 |
| C ₁₀ H ₁₃ NO ₃ | Me ₃ CCH ₂ | Me | HOCH ₂ | H | 138-141 | 60 | 351 |
| C ₁₁ H ₁₃ NO ₂ | Me | Me | H | Ph | From ephedrine: 57-58, 175-177 (7-8); from pseudoephedrine: 56-56.5, 160 (6-9); from isoephedrine: 72-73 | .. | 166 |
| C ₁₁ H ₁₄ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ CH ₂ | Me | HOCH ₂ | H | 119-120 | 80 | 351 |
| C ₁₁ H ₁₅ NO ₃ | PhCH ₂ | Me | HOCH ₂ | H | 92-93 | .. | 351 |
| C ₁₁ H ₂₁ NO ₃ | Me(CH ₂) ₈ | Me | HOCH ₂ | H | 148-150 (0.05) | 86 | 351 |
| | Et ₂ CHCH ₂ | Me | HOCH ₂ | H | 48-49, 138-139 (0.01) | .. | 351 |
| C ₁₂ H ₁₇ NO ₄ | PhCH(OH)CH ₂ | Me | HOCH ₂ | H | 106-107 | 6 | 351 |
| C ₁₃ H ₁₅ N ₂ O ₄ | PhCH ₂ | Me | H ₂ NCO ₂ CH ₂ | H | 132 | .. | 351 |
| C ₁₃ H ₁₅ N ₄ O ₆ | 5-Nitro-2-furfurylideneamino | H | H | N-Morpholino-methyl | 206 | .. | 32 |
| C ₁₃ H ₁₇ NO ₄ | <i>p</i> -MeOC ₆ H ₄ CH ₂ | Me | HOCH ₂ | H | 132-134 | 90 | 351 |
| C ₁₃ H ₁₉ N ₃ O ₃ | PhCH=N | H | H | N-Morpholino-methyl | 166-167 | .. | 32 |
| C ₁₅ H ₂₁ NO ₆ | 3,4,5-(MeO) ₃ C ₆ H ₂ CH ₂ | Me | HOCH ₂ | H | 136-139, 225-230 (0.02) | .. | 351 |

^a R₅ = H.

TABLE VII

2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND ESTERS OF TRICHLOROACETIC ACID

| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|---|---------------------|-------------------|---------|----------|
| C ₆ H ₉ NO ₃ | HOCH ₂ CH ₂ | H | 150-155 (0.25) | 92 | 102, 299 |
| C ₁₀ H ₉ NO ₂ Cl ₂ | 2,6-Cl ₂ C ₆ H ₃ CH ₂ | H | 115.8-118.1 | 57 | 306, 518 |
| | 3,4-Cl ₂ C ₆ H ₃ CH ₂ | H | 68.0-69.6 | 84 | 306, 518 |
| | 2,4-Cl ₂ C ₆ H ₃ CH ₂ | H | 72.2-74.3 | 79 | 306 |
| C ₁₀ H ₁₀ NO ₂ Cl | <i>o</i> -ClC ₆ H ₄ CH ₂ | H | 70.0-72.1 | 75 | 306, 518 |
| | <i>p</i> -ClC ₆ H ₄ CH ₂ | H | 72.1-73.5 | 48 | 306, 518 |
| C ₁₀ H ₁₀ N ₂ O ₄ | <i>p</i> -O ₂ NC ₆ H ₄ CH ₂ | H | 148.0-150.3 | 90 | 306, 518 |
| C ₁₀ H ₁₁ NO ₂ | PhCH ₂ | H | 78.3-79.2 | 40 | 306 |
| C ₁₀ H ₁₁ NO ₃ | <i>p</i> -HOC ₆ H ₄ CH ₂ | H | 128.2-129.2 | 52 | 306 |
| C ₁₀ H ₁₃ N ₂ O ₂ Cl | <i>p</i> -H ₃ N ⁺ C ₆ H ₄ CH ₂ Cl ⁻ | H | 190.9-192.1 | .. | 306 |
| C ₁₁ H ₁₁ NO ₂ Cl ₂ | 2,4-Cl ₂ C ₆ H ₃ CH ₂ | Me | 75.4-77.6 | .. | 518 |
| C ₁₁ H ₁₁ NO ₄ | 3,4-CH ₂ O ₂ C ₆ H ₃ CH ₂ | H | 59.3-62.2 | 63 | 306, 518 |
| C ₁₁ H ₁₃ NO ₂ | <i>p</i> -MeC ₆ H ₄ CH ₂ | H | 160-162 (0.03) | 92 | 306 |
| C ₁₂ H ₁₅ NO ₃ | <i>p</i> -EtOC ₆ H ₄ CH ₂ | H | 63.4-66.1 | 68 | 306, 518 |
| C ₁₂ H ₁₅ NO ₄ | 3,4-(MeO) ₂ C ₆ H ₃ CH ₂ | H | 59.3-62.2 | 62 | 306, 518 |
| C ₁₂ H ₁₆ N ₄ O ₆ | 5-Nitro-2-furfurylideneamino | N-Morpholino-methyl | 205-206 dec | .. | 312 |
| C ₁₃ H ₁₇ NO ₂ | <i>p</i> - <i>i</i> -PrC ₆ H ₄ CH ₂ | H | 47.5-49.1 | 59 | 306 |
| C ₁₄ H ₁₉ NO ₂ | <i>p</i> - <i>n</i> -BuC ₆ H ₄ CH ₂ | H | 170-175 (0.04) | 87 | 306, 518 |

^a R₂ = R₃ = R₆ = H.

8. Use of Miscellaneous Cyclizing Reagents with β -Amino Alcohols

a. Carbonyl Sulfide or Carbon Monoxide and Sulfur (Table VIII)

Among the gaseous cyclizing reagents, both carbonyl sulfide COS (35) and its equivalent, carbon monoxide

and sulfur (20), have been used. In both cases pressure is used along with methanol as solvent. In the case of carbonyl sulfide, the reaction is catalyzed by cumene hydroperoxide, suggesting a free-radical reaction. No work has been reported on the mechanism or stereochemistry of the reaction, however. Only

TABLE VIII

| 2-OXAZOLIDONES PREPARED FROM β -AMINO ALCOHOLS AND CARBONYL SULFIDE OR CARBON MONOXIDE AND SULFUR | | | | | | |
|---|-------------------|-------------------|---------|---------|--------|-----|
| Empirical formula ^a | R ₂ | R ₃ | Mp, °C | % yield | Method | Ref |
| C ₃ H ₅ NO ₂ | H | H | ... | 23 | COS | 35 |
| | H | H | 88-90 | 90 | CO + S | 20 |
| C ₄ H ₉ NO ₂ | Et | H | ... | .. | CO + S | 20 |
| C ₆ H ₉ NO ₄ | HOCH ₂ | HOCH ₂ | 106-110 | .. | CO + S | 20 |

^a R₁ = R₄ = R₅ = H.

a few 2-oxazolidones have been prepared by this method.

b. Carbon Tetrachloride

Two groups of workers have reported the use of carbon tetrachloride as the cyclizing reagent for ephedrine. One group (256) obtained a small yield of 3,4-dimethyl-5-phenyl-2-oxazolidone, mp 91-92° (EtOH), using a sunlamp to bring about the reaction. They also found that the yield could be increased by addition of water.

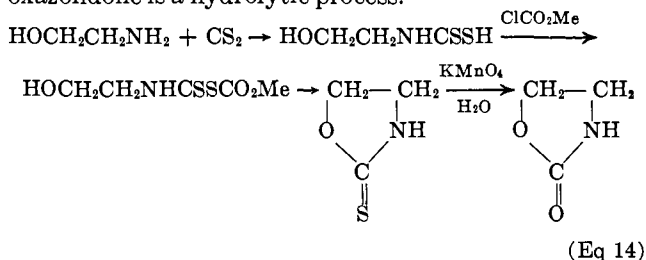
The other group (415) carried out the reaction under nitrogen in the presence of copper and oxygen. They also obtained 3,4-dimethyl-5-phenyl-2-oxazolidone from ephedrine. It has been pointed out that carbon tetrachloride acts as a hydrogen acceptor to form hydrogen chloride and chloroform. No mechanistic details are known, and only one synthetic example is reported.

c. Cyanogen Bromide and Base

The β -amino alcohol, diethanolamine, has been treated with BrCN and then potassium hydroxide to yield a small amount of 3-(β -hydroxyethyl)-2-oxazolidone (331).

d. Carbon Bisulfide and Methyl Chloroformate

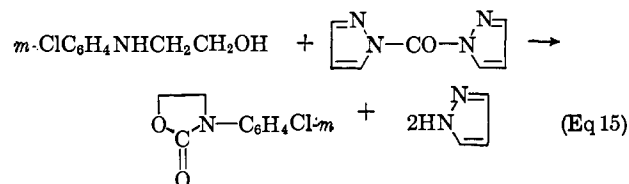
2-Oxazolidone has been prepared (470) by the reaction of β -aminoethanol first with carbon bisulfide followed by methyl chloroformate. This yields the 2-thione which on treatment with aqueous potassium permanganate is converted to the 2-oxazolidone (Eq 14). In the reviewers' opinion the potassium permanganate is unnecessary; the conversion of the thione to the 2-oxazolidone is a hydrolytic process.



e. N,N'-Carbonyldiimidazole

There is only one literature report of the preparation of a 2-oxazolidone from a β -amino alcohol using

N,N'-carbonyldiimidazole as the cyclizing reagent (Eq 15) (599).



C. FROM β -AMINOALKYLSULFURIC ACIDS (TABLE IX)

The feasibility of synthesizing 2-oxazolidones from β -aminoalkylsulfuric acids using an inorganic carbonate or bicarbonate in the presence of base as cyclizing reagent has been shown in a few cases. Both potassium carbonate (118) and sodium bicarbonate (484, 561) in the presence of sodium hydroxide have been used.

TABLE IX

2-OXAZOLIDONES PREPARED FROM β -AMINOALKYLSULFURIC ACIDS AND INORGANIC CARBONATES

| Empirical formula ^a | R ₁ | Bp (mm) or mp, °C | % yield | Ref |
|---|-----------------------------------|-------------------|---------|---------------|
| C ₃ H ₅ NO ₂ | H | ... | 90 | 118, 484, 561 |
| C ₅ H ₉ NO ₂ | HOCH ₂ CH ₂ | 170 (0.5) | .. | 484, 561 |
| C ₉ H ₉ NO ₂ | Ph | 123 | .. | 484, 561 |

^a R₂ = R₃ = R₄ = R₅ = H.

D. FROM β -HALOAMINES (TABLE X)

Gabriel (189) was the first to prepare 2-oxazolidone. He employed the reaction of silver carbonate with β -bromoethylamine hydrobromide. More recently, sodium carbonate or sodium bicarbonate in the presence of sodium hydroxide has been used (27, 28, 407). The reaction has had only limited study.

E. FROM β -HALO ALCOHOLS (HALOHYDRINS)

Only a modest amount of work has been reported to date on the preparation of 2-oxazolidones from β -halo alcohols. It seems worthwhile, however, to classify the few examples in the literature on the basis of the cyclizing reagent used in view of the ready availability of halohydrins and the cyclizing reagents employed.

TABLE X
 2-OXAZOLIDONES PREPARED FROM β -HALOAMINES AND INORGANIC CARBONATES

| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|-----------------------------------|----------------|-------------------|---------|--------|
| C ₃ H ₅ NO ₂ | H | H | 90–91 (EtOH) | .. | 189 |
| C ₅ H ₉ NO ₂ Cl | ClCH ₂ CH ₂ | H | 114 (0.3) | 95 | 27, 28 |
| C ₅ H ₉ NO ₃ | HOCH ₂ CH ₂ | H | 125–140 (0.1) | .. | 28 |
| C ₆ H ₁₀ NO ₂ Cl | Cl(CH ₂) ₃ | H | 132–135 (0.5) | 82 | 27 |
| | ClCH(Me)CH ₂ | H | 107–108 (0.5) | 84 | 27 |
| C ₇ H ₁₂ NO ₂ Cl | Cl(CH ₂) ₄ | Me | 112–114 (0.1) | 50 | 27 |

^a R₂ = R₃ = R₅ = H.

 TABLE XI
 2-OXAZOLIDONES PREPARED FROM β -HALO ALCOHOLS AND UREA

| Empirical formula ^a | R ₄ | Mp, °C | % yield | Ref |
|---|---|------------------|---------|-----|
| C ₁₁ H ₁₃ NO ₃ | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 128–129 (EtOAc) | .. | 44 |
| C ₁₁ H ₁₃ NO ₄ | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 140.5–142 (EtOH) | .. | 323 |
| C ₁₂ H ₁₅ NO ₅ | 3,5-(MeO) ₂ C ₆ H ₄ OCH ₂ | 124–125 | .. | 427 |
| C ₁₃ H ₁₇ NO ₃ | 2,3,5-Me ₃ C ₆ H ₂ OCH ₂ | 125–126 | 60 | 427 |
| | 3,4,5-Me ₃ C ₆ H ₂ OCH ₂ | 129–132 | .. | 427 |

^a R₁ = R₂ = R₃ = R₅ = H.

 TABLE XII
 2-OXAZOLIDONES PREPARED FROM β -HALO ALCOHOLS AND URETHANS

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Mp, °C | % yield | Ref |
|---|---------------------------------|----------------|----------------|----------------|---------|-----|
| C ₁₀ H ₁₀ N ₂ O ₂ | PhCH=N | H | H | 142–143 (EtOH) | 78 | 481 |
| C ₁₀ H ₁₁ N ₃ O ₅ | 5-Nitro-2-furfuryli-deneamino | Me | Me | 140.5–143.0 | 66 | 481 |
| C ₁₅ H ₂₃ NO ₂ | C ₁₂ H ₂₅ | H | H | 62 | 53 | 530 |

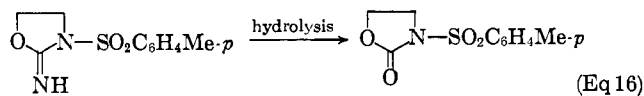
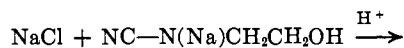
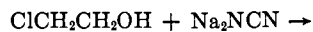
^a R₃ = R₅ = H.

1. Use of Urea (Table XI)

Cyclization of β -halo alcohols with urea to form 2-oxazolidones has been reported by several investigators (44, 323, 427).

2. Use of Sodium Cyanamide

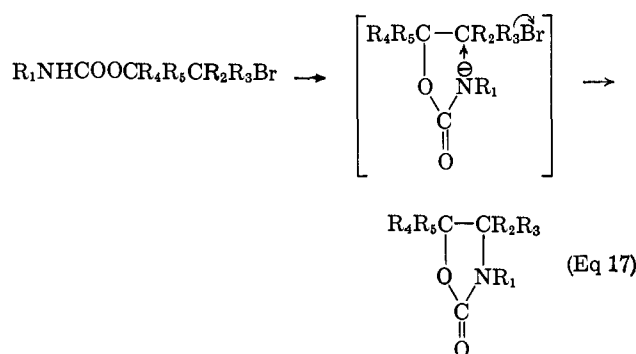
Many years ago, Fromm and Honold (182) obtained a derivative of 2-oxazolidone by the sequence shown in Eq 16.



3. Use of Urethans (Table XII)

Urethans have been used to cyclize β -halo alcohols although examples are still limited. The reaction is carried out in the presence of base, such as alcoholic potassium hydroxide (530) and sodium ethoxide (481),

and proceeds first by transesterification followed by cyclization (Eq 17).



4. Use of Inorganic Cyanates (Table XIII)

There are two references in the literature (44, 184) to the reaction of inorganic cyanates with β -halo alcohols to form 2-oxazolidones. In one (184) the reaction was carried out in dimethylformamide, with or without the addition of iodide ion, and methyl sulfate. In the other (44), an epoxide ring was first opened with aqueous hydrochloric acid to give the chlorohydrin which then underwent displacement of chloride by cyanate ion (Eq 18). The intermediate isocyanate

TABLE XIII
 2-OXAZOLIDONES PREPARED FROM β -HALO ALCOHOLS AND INORGANIC CYANATES

| Empirical formula ^a | R ₄ | R ₅ | Mp, °C | % yield | Ref |
|--|--|----------------|-----------------------------------|---------|-----|
| C ₄ H ₅ NO ₂ | H | H | 79-80 (dioxane-Et ₂ O) | 93 | 184 |
| C ₆ H ₇ NO ₂ | Me | H | ... | 79 | 184 |
| C ₈ H ₁₁ NO ₂ | -(CH ₂) ₅ - | H | 101-102 (dioxane) | 44 | 184 |
| C ₉ H ₁₀ NO ₂ | Ph | H | ... | .. | 184 |
| C ₁₀ H ₁₀ NO ₂ Cl | <i>o</i> -ClC ₆ H ₄ OCH ₂ | H | 151 (EtOAc) | .. | 44 |
| C ₁₁ H ₁₃ NO ₂ | <i>o</i> -MeC ₆ H ₄ OCH ₂ | H | 128-129 (EtOAc) | .. | 44 |

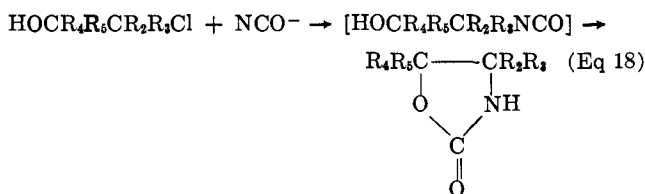
^a R₁ = R₂ = R₃ = H.

 TABLE XIV
 2-OXAZOLIDONES PREPARED FROM β -HALOETHANOLS AND PHOSGENE PLUS PRIMARY AMINES

| Empirical formula ^a | R ₁ | Bp (mm) or mp, °C | % yield | Ref |
|--|--|-----------------------------|---------|--------|
| C ₂ H ₄ NO ₂ Cl | Cl | 122 | 82 | 66 |
| C ₇ H ₁₂ NO ₂ | <i>n</i> -C ₄ H ₉ | 132 (3) | 70 | 66 |
| C ₈ H ₁₅ NO ₂ | <i>n</i> -C ₆ H ₁₁ | 145 (4) | 68 | 66 |
| C ₉ H ₉ NO ₂ Cl | <i>o</i> -ClC ₆ H ₄ | 185-188 (3), 192-194 (7) | 82 | 5, 66 |
| | <i>m</i> -ClC ₆ H ₄ | 53-54 | 73 | 66 |
| | <i>p</i> -ClC ₆ H ₄ | 121-122, 118.5-119.0 (EtOH) | 80 | 5, 66 |
| C ₉ H ₉ NO ₂ | Ph | ... | .. | 4, 379 |
| C ₉ H ₁₇ NO ₂ | <i>n</i> -C ₈ H ₁₇ | 176 (1) | 82 | 66 |
| C ₁₀ H ₁₁ NO ₂ | <i>o</i> -MeC ₆ H ₄ | 180-185 (3) | .. | 5 |
| | <i>p</i> -MeC ₆ H ₄ | 91 (EtOH) | ... | 5 |
| C ₁₁ H ₁₃ NO ₂ | <i>p</i> -EtOC ₆ H ₄ | 96 (EtOH-Et ₂ O) | ... | 4, 5 |
| C ₁₃ H ₁₁ NO ₂ | α -Naphthyl | 130 | 78 | 66 |

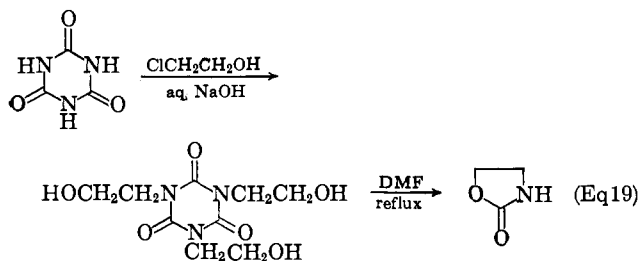
^a R₂ = R₃ = R₄ = R₅ = H.

cannot be isolated as it immediately undergoes ring closure with the neighboring hydroxyl group.



5. Use of Cyanuric Acid

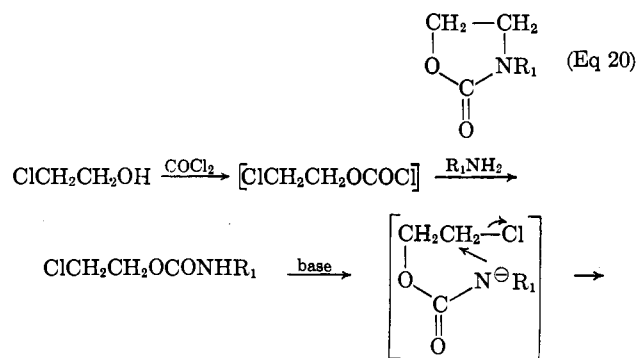
Cyanuric acid, the cyclic trimer of isocyanic acid, HNCO, has been used to cyclize β -chloroethanol in basic medium (455). Hydrogen chloride is eliminated to form the tris(hydroxyethyl) derivative, which on heating collapses to 2-oxazolidone in high yield (Eq 19).



6. Use of Phosgene plus Amines (Table XIV)

Another early method is the reaction of phosgene and aniline with β -chloroethanol to produce β -chloro-

ethyl N-phenylcarbamate, which is cyclized by boiling in potassium hydroxide solution (379) (Eq 20).



F. FROM 1,2-GLYCOLS

1. Use of Urea (Table XV)

When 2 moles of urea are heated with 1 mole of a 1,2 glycol, 2-oxazolidones are obtained in fairly good, but sometimes variable yields. The reaction has received extensive study. The following mechanism has been suggested (325) (Eq 21a-e).

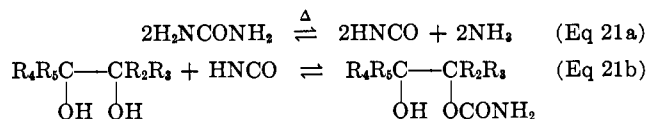
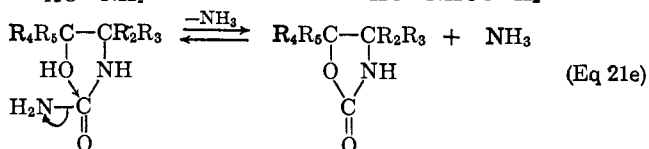
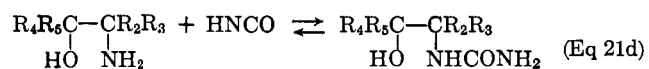
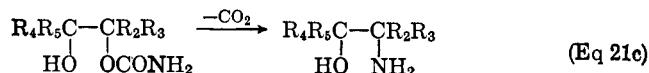


TABLE XV
 2-OXAZOLIDONES PREPARED FROM 1,2-GLYCOLS AND UREA

| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|----------------|---|---|---------|----------------------|
| C ₃ H ₅ NO ₂ | H | H | 91, 87-89 (CHCl ₃) | .. | 260, 406 |
| C ₁₀ H ₉ NO ₃ Cl ₃ | H | 2,4,6-Cl ₃ C ₆ H ₂ OCH ₂ | ... | .. | 319 |
| C ₁₀ H ₉ NO ₃ Cl ₂ | H | 2,4-Cl ₂ C ₆ H ₃ OCH ₂ | 128-130 (EtOAc) | 42 | 319, 325 |
| C ₁₀ H ₁₀ NO ₃ Cl | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | 147-148 (EtOAc) | 48 | 325 |
| | H | <i>m</i> -ClC ₆ H ₄ OCH ₂ | 96.5-97 (EtOAc) | 76 | 325 |
| | H | <i>p</i> -ClC ₆ H ₄ OCH ₂ | 143.5-146 (EtOAc) | 59 | 325 |
| C ₁₀ H ₁₀ NO ₃ Br | H | <i>p</i> -BrC ₆ H ₄ OCH ₂ | 153-154 (EtOAc) | 47 | 325 |
| C ₁₀ H ₁₁ NO ₃ | H | PhOCH ₂ | 120.5-122 (EtOAc) | 49 | 325 |
| C ₁₀ H ₁₁ NO ₄ | H | <i>o</i> -HOC ₆ H ₄ OCH ₂ | 84-86 (EtOAc) | 20 | 325 |
| C ₁₁ H ₁₂ NO ₃ F | H | 2-Me-4-FC ₆ H ₃ OCH ₂ | ... | .. | 319 |
| | H | 3-Me-4-FC ₆ H ₃ OCH ₂ | ... | .. | 320 |
| C ₁₁ H ₁₂ NO ₃ Cl | H | 2-Me-5-ClC ₆ H ₃ OCH ₂ | 104-104.5 (EtOAc) | 57 | 319, 325 |
| | H | 2-Me-3-ClC ₆ H ₃ OCH ₂ | 124.0-125.5 (EtOAc) | 35 | 325 |
| | H | 3-Me-4-ClC ₆ H ₃ OCH ₂ | 135-137 (EtOAc) | 36 | 325 |
| C ₁₁ H ₁₂ NO ₃ Br | H | 2-Me-4-BrC ₆ H ₃ OCH ₂ | ... | .. | 319 |
| | H | 3-Me-4-BrC ₆ H ₃ OCH ₂ | ... | .. | 320 |
| C ₁₁ H ₁₂ NO ₃ | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 127-129, 124.5-125.5 (MeOH) | 94 | 44, 325 |
| | H | <i>m</i> -MeC ₆ H ₄ OCH ₂ | 102-103, 225-240 (0.35) | 54 | 325 |
| | H | <i>p</i> -MeC ₆ H ₄ OCH ₂ | 131-131.5 (EtOAc) | 58 | 325 |
| C ₁₁ H ₁₂ NO ₃ Cl | Me | <i>o</i> -ClC ₆ H ₄ OCH ₂ | 79-81 | .. | 12 |
| | Me | <i>m</i> -ClC ₆ H ₄ OCH ₂ | ... | .. | 12 |
| C ₁₁ H ₁₂ NO ₄ | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 140.5-142.0 (EtOH); 141-143 (H ₂ O); 143-145 (95% EtOH) | 67 | 12, 321, 323, 325 |
| | H | <i>m</i> -MeOC ₆ H ₄ OCH ₂ | 121-123, 125.0-126.5 (EtOAc) | 48 | 12, 325 |
| | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | 135-136 (EtOAc) | 50 | 325 |
| C ₁₂ H ₁₄ NO ₃ Cl | Me | 3-Me,4-ClC ₆ H ₃ OCH ₂ | ... | .. | 320 |
| C ₁₂ H ₁₄ NO ₃ | Me | <i>m</i> -MeC ₆ H ₄ OCH ₂ | 73.5 | .. | 12 |
| | H | 3,4-Me ₂ C ₆ H ₃ OCH ₂ | 116-117 (EtOAc) | 37 | 325 |
| | H | 3,5-Me ₂ C ₆ H ₃ OCH ₂ | 121.5-123.0 (EtOAc), 220-225 (1.5) | 79 | 325, 437 |
| | H | 2,6-Me ₂ C ₆ H ₃ OCH ₂ | 104-105 (EtOAc), 220-235 (0.35) | 74 | 319, 325 |
| C ₁₂ H ₁₄ NO ₄ | Me | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 72.5-75.0 (C ₄ H ₉ -Et ₂ O) | .. | 12 |
| | Me | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | ... | .. | 12 |
| | H | <i>o</i> -EtOC ₆ H ₄ OCH ₂ | 98-100, 105-106 | 42 | 12, 260 |
| C ₁₂ H ₁₆ NO ₅ | H | 2,6-(MeO) ₂ C ₆ H ₃ OCH ₂ | 104-105, 117.5-118.5 (EtOAc) | 52 | 319, 324, 325 |
| | H | 3,5-(MeO) ₂ C ₆ H ₃ OCH ₂ | 124-125 (EtOAc), 245-257 (0.15) | 75 | 325, 437 |
| C ₁₃ H ₁₆ NO ₃ Cl | H | 2-Pr-6-ClC ₆ H ₃ OCH ₂ | ... | .. | 319 |
| | Et | 3-Me-4-ClC ₆ H ₃ OCH ₂ | 95.5-96.0 (<i>i</i> -Pr ₂ O) | .. | 320 |
| C ₁₃ H ₁₆ NO ₃ Br | H | 3-Pr-4-BrC ₆ H ₃ OCH ₂ | ... | .. | 320 |
| C ₁₃ H ₁₆ NO ₄ Cl | H | 2-PrO-6-ClC ₆ H ₃ OCH ₂ | ... | .. | 319 |
| C ₁₃ H ₁₇ NO ₃ | H | 3,4,5-Me ₃ C ₆ H ₂ OCH ₂ | 129-132 | .. | 437 |
| | H | 2,3,5-Me ₃ C ₆ H ₂ OCH ₂ | 125-126 (EtOAc) | 60 | 325, 437 |
| C ₁₃ H ₁₇ NO ₄ | Et | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 175-178 (0.1) | .. | 12 |
| | H | 2-MeO-4-BrC ₆ H ₃ OCH ₂ | 106-108 | 63 | 260 |
| C ₁₄ H ₁₇ NO ₅ | H | 3,4,5-(MeO) ₃ C ₆ H ₂ OCH ₂ | 129-132 (EtOAc), 265-280 (0.15) | 60 | 325 |
| C ₁₄ H ₁₇ NO ₄ | H | 2-MeO-6-(CH ₂ =CHCH ₂)C ₆ H ₃ OCH ₂ | ... | .. | 319 |
| C ₁₄ H ₁₈ NO ₃ Cl | Pr | 3-Me-4-ClC ₆ H ₃ OCH ₂ | ... | .. | 320 |
| C ₁₄ H ₁₉ NO ₃ | H | 2,6-Et ₂ C ₆ H ₃ OCH ₂ | ... | .. | 319 |
| C ₁₄ H ₁₉ NO ₄ | H | <i>p</i> -BuOC ₆ H ₄ OCH ₂ | 139.5-141.5 (EtOAc) | 45 | 325 |
| | H | <i>o</i> -BuOC ₆ H ₄ OCH ₂ | 62-63 (EtOAc), 235-255 (0.1) | 71 | 325 |
| C ₁₆ H ₂₀ NO ₅ | H | 2,6-(PrO) ₂ C ₆ H ₃ OCH ₂ | ... | .. | 319 |

^a R₂ = R₃ = R₅ = H.



2. Use of Urethan (Table XVI)

Cyclization of 1,2-glycols to 2-oxazolidones has also been effected by reaction with urethan in the presence of bases, such as sodium ethoxide (300) and aluminum isopropoxide (108) (Eq 22). Not much work has been done on this reaction which has the advantage of simplicity.

TABLE XVI

2-OXAZOLIDONES PREPARED FROM 1,2-GLYCOLS AND URETHAN

| Empirical formula ^a | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|-----------------------|---------|--------------|
| C ₁₁ H ₁₃ NO ₂ | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 130-131 (EtOH) | .. | 59, 105, 300 |
| C ₁₁ H ₁₃ NO ₄ | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 145-146 (EtOH) | .. | 59, 300 |
| C ₁₃ H ₁₇ NO ₄ | 2-MeO-4-EtOC ₆ H ₃ OCH ₂ | ... | .. | 108 |
| C ₁₄ H ₁₇ NO ₄ | 2-MeO-4-(MeCH=CH)C ₆ H ₃ OCH ₂ | 116-117 | .. | 108 |
| | 2-MeO-4-(CH ₂ =CHCH ₂)C ₆ H ₃ OCH ₂ | 109-110 | .. | 108 |
| C ₁₄ H ₁₉ NO ₄ | 2-MeO-4-PrC ₆ H ₃ OCH ₂ | 103-104 | .. | 108 |
| C ₁₆ H ₁₅ NO ₂ | <i>o</i> -PhC ₆ H ₄ OCH ₂ | 99-100, 205-230 (0.1) | 48 | 108 |
| | <i>p</i> -PhC ₆ H ₄ OCH ₂ | 195-196 | .. | 108 |

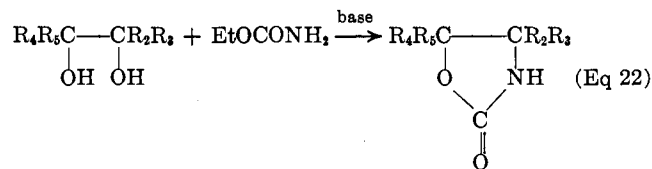
^a R₁ = R₂ = R₃ = R₅ = H.

TABLE XVII

2-OXAZOLIDONES PREPARED FROM EPOXIDES AND CYANURIC ACID

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|---|------------------------------------|------------------------------------|--|---------|---------------|
| C ₃ H ₅ NO ₂ | H | H | H | 85-87 (MeOH), 89-90, 130-140 (1-2) | 90 | 111, 179, 311 |
| C ₄ H ₇ NO ₂ | H | H | Me | 111-113 (1), 113-118 (3) | .. | 111, 311 |
| C ₄ H ₇ NO ₂ | H | H | CH ₂ =CH | 41-44 (Et ₂ O), 125-130 (0.1) | .. | 310 |
| C ₅ H ₉ NO ₂ | HOCH ₂ CH ₂ | H | H | 145-165 (1) | .. | 177 |
| C ₆ H ₁₁ NO ₂ | HOCH ₂ CH ₂ | H | Me | 123-128 (0.1) | .. | 177 |
| C ₉ H ₉ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | H | H | 119-120 | .. | 134 |
| C ₉ H ₉ NO ₂ | Ph | H | H | 119-120 (THF-hexane) | .. | 134 |
| C ₁₀ H ₁₁ NO ₂ | Ph | (Me) ^b | (Me) ^b | 81 | .. | 134 |
| C ₁₁ H ₁₁ NO ₂ | Ph | (CH ₂ =CH) ^b | (CH ₂ =CH) ^b | 87, 171-176 (3.5) | .. | 134 |
| C ₁₃ H ₁₅ NO ₂ | Ph | -(CH ₂) ₄ - | -(CH ₂) ₄ - | 168-173 (0.3) | .. | 134 |
| C ₁₄ H ₁₇ NO ₂ | Ph | (4-Pentenyl) ^b | (4-Pentenyl) ^b | 161-163 (0.15) | .. | 134 |

^a R₃ = R₅ = H. ^b Position of substituent in doubt.



G. FROM 1,2-DIHALIDES

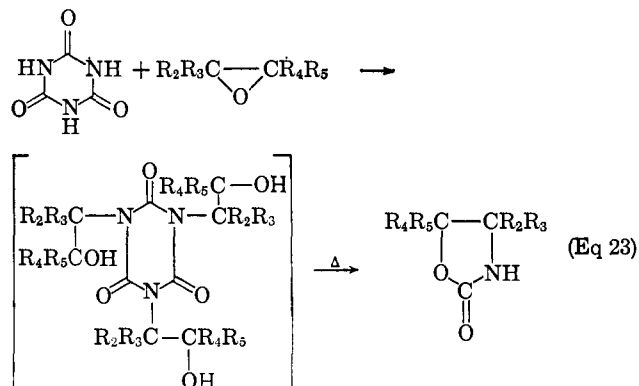
A single patent (533) reports the preparation of 2-oxazolidone, mp 88° [EtOH or (CH₂Cl)₂] and bp 160-170° (5 mm), in 39% yield by the high-temperature, high-pressure reaction of 1,2-dichloroethane, ammonia, and carbon dioxide. The ammonia is generated *in situ* from ammonium sesquicarbonate.

H. FROM EPOXIDES

1. Use of Cyanuric Acid (Table XVII)

2-Oxazolidones have been prepared by the reaction of epoxides with cyanuric acid (*s*-triazinetrione). Both heat and base are necessary for the success of the reaction; dimethylformamide is a solvent of choice. It has been suggested that the acidic hydrogens bonded to the nitrogen atoms of cyanuric acid open the epoxide ring to form a triply substituted isocyanurate with hydroxyl groups β to the ring as shown in the bracketed formula below. Subsequently, 3 moles of 2-oxazolidone are formed by pyrolytic collapse of the cyanuric acid ring (Eq 23). This mechanism readily accounts

for the preparation of 2-oxazolidones in which R₁ = H, but when R₁ is a substituent group a different mechanism must apply (see section IIH2 below for the reaction of epoxides with organic isocyanates).

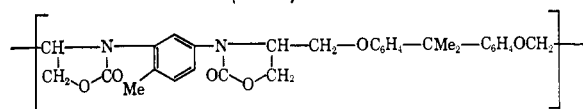
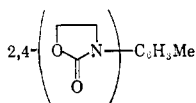


2. Use of Organic Isocyanates (Table XVIII) and Inorganic Cyanates

The reaction of epoxides with organic isocyanates has received much attention recently. The reaction has been carried out in solvents, such as dimethylformamide, acetonitrile, dioxane, etc. (491) and without solvent (214). Catalysts employed are secondary amines (592), tertiary amines (215), the halide salts of amines (269), carboxylate anions (135), zinc

TABLE XVIII
2-OXAZOLIDONES PREPARED FROM EPOXIDES AND ORGANIC ISOCYANATES

| Empirical formula ^a | R ₁ | R ₂ | R ₃ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|-------------------|---|--|---------|-----------------------------|
| C ₅ H ₉ NO ₂ | Et | H | H | 129-130 (10), 65-68 (0.15) | 26 | 269, 398, 491 |
| C ₉ H ₉ NO ₂ | Ph | H | H | 116 (THF-hexane), 118-121, 119.8-120.2 (dioxane), 121-122, 196 (2) | 92 | 135, 214-216, 269, 398, 491 |
| C ₁₀ H ₁₁ NO ₂ | Ph | H | Me | 79.5-81.5 (EtOH) | 64 | 269, 491 |
| | Ph | (Me) ^b | (Me) ^b | 81-83 | .. | 398 |
| C ₁₃ H ₁₅ NO ₂ | Ph | H | CH ₂ =CHCH ₂ OCH ₂ | 176 (0.06) | 76 | 214 |
| C ₁₆ H ₁₉ NO ₂ | Cyclohexyl | H | Ph | 95-96 (pet. ether) | 90 | 214 |
| C ₁₄ H ₁₅ NO ₂ | PhCH ₂ | H | Ph | 210-220 (0.4) | 39 | 214 |
| C ₁₆ H ₁₅ NO ₂ | Ph | H | PhOCH ₂ | 134.5-136.5, 137-138 (C ₆ H ₆), 233-234 (0.5) | 88 | 215, 479, 491, 592 |
| C ₁₆ H ₂₁ NO ₂ | Cyclohexyl | H | PhOCH ₂ | 147.0-147.5 (pet. ether), 200-202 (0.2) | 96 | 214 |
| C ₁₉ H ₂₉ NO ₂ | Ph | H | <i>n</i> -C ₁₀ H ₂₁ | 68.5-69.7 (pet. ether) | 25 | 269 |
| C ₂₂ H ₃₄ NO ₂ | <i>n</i> -C ₁₂ H ₂₅ | H | PhOCH ₂ | 62 (EtOH), 231-232 (0.2) | 64 | 214 |



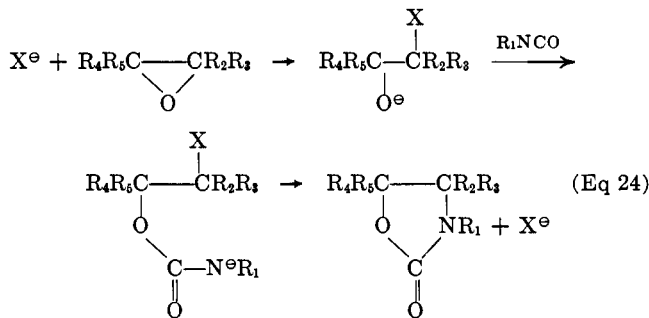
137.5 (EtOH, then C₆H₆) 53 491

175-185 91 452

^a R₄ = R₅ = H. ^b Position of substituent in doubt.

chloride, ferric chloride, and lithium chloride. Catalysts are not essential, however (398). This reaction has been used to prepare condensation polymers from diepoxides and diisocyanates (452). The poly(2-oxazolidones) are high melting.

A suggested mechanism using halide ion catalysis is formulated in Eq 24 (491). If an isocyanate trimer is employed, it may dissociate to the monomeric isocyanate under the reaction conditions.



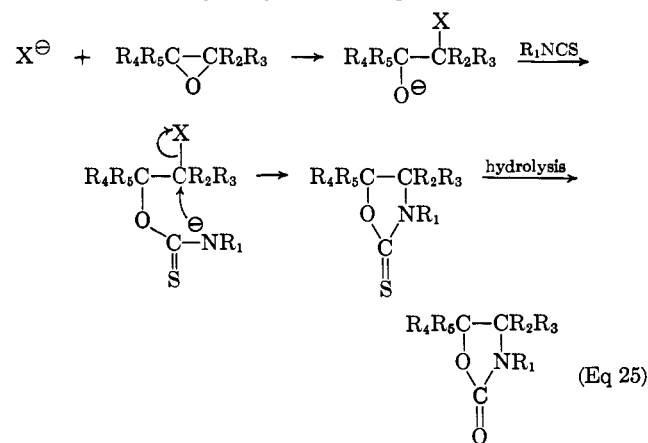
Only two reports could be found (407, 534) on the preparation of a 2-oxazolidone by reaction of an inorganic cyanate (KNCO) with an epoxide (epichlorohydrin). This is the earliest known 2-oxazolidone synthesis. The position of the substituent on the 2-oxazolidone ring has been questioned. The product, mp 105°, has been reported as 4- or 5-chloromethyl-2-oxazolidone (407, 534).

3. Use of Isothiocyanates (Table XIX)

The preparation of 2-oxazolidones directly from epoxides and isothiocyanates has been reported by

two groups (164, 169). Triethylamine, tetraethylammonium bromide (164), and lithium chloride (169) have been used as catalysts.

A proposed mechanism is given in Eq 25. It suggests the formation of an intermediate 2-oxazolidine-thione which is hydrolyzed to the product.



4. Use of Urea and Substituted Ureas (Table XX)

Urea has been used to cyclize epoxides to 2-oxazolidones (Eq 26). Little work appears to have been done

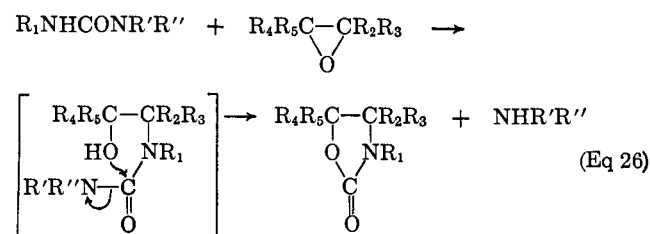


TABLE XIX
 2-OXAZOLIDONES PREPARED FROM EPOXIDES AND ISOTHIOCYANATES

| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|--|----------------|--------------------|---|---------|----------|
| C ₉ H ₇ NO ₂ | Ph | H | 121 (CH ₂ Cl ₂ -pet. ether) | 60 | 164, 169 |
| C ₁₆ H ₁₀ NO ₂ Cl | Ph | ClCH ₂ | 103 | 85 | 164 |
| C ₁₀ H ₁₁ NO ₂ | Ph | Me | 81.5 | 45 | 164 |
| C ₁₆ H ₁₅ NO ₂ | Ph | PhOCH ₂ | 137-138 (CH ₂ Cl ₂ -pet. ether) | 25 | 169 |

^a R₂ = R₃ = R₅ = H.

 TABLE XX
 2-OXAZOLIDONES PREPARED FROM EPOXIDES AND UREA

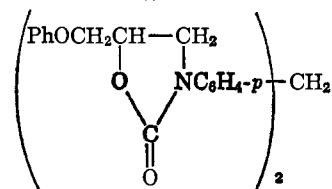
| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | Ref |
|---|----------------|---|--------------------------------------|-----|
| C ₈ H ₅ NO ₂ | H | H | 89 (EtOH) | 394 |
| C ₁₀ H ₁₁ NO ₂ | H | PhOCH ₂ | 124, 225-227 (5) | 393 |
| C ₁₁ H ₁₃ NO ₂ | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 125-127 (CHCl ₃ -ligroin) | 44 |
| C ₁₁ H ₁₃ NO ₄ | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 140.5-142.0 (EtOH) | 323 |
| C ₁₆ H ₁₅ NO ₂ | Ph | PhOCH ₂ | ... | 263 |

^a R₂ = R₃ = R₅ = H.

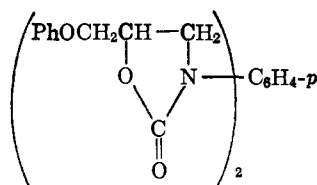
 TABLE XXI
 2-OXAZOLIDONES PREPARED FROM EPOXIDES AND URETHAN OR SUBSTITUTED URETHANS

| Empirical formula ^a | R ₁ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|--|--------------------------------|---------|----------|
| C ₈ H ₇ N ₂ O ₅ | 5-Nitro-2-furfurylideneamino | H | ... | ... | 391 |
| C ₁₀ H ₁₀ NO ₃ Cl | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | 146.9-151.0 (EtOAc) | ... | 328 |
| C ₁₁ H ₁₃ NO ₃ | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 128-129 (EtOH) | ... | 44 |
| C ₁₁ H ₁₃ NO ₄ | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 140.5-142.0 (EtOH) | ... | 323, 328 |
| | | | 141.4-141.9 (H ₂ O) | | |
| C ₁₂ H ₁₅ NO ₃ | H | 3,5-Me ₂ C ₆ H ₄ OCH ₂ | ... | ... | 328 |
| C ₁₄ H ₁₅ N ₂ O ₂ | 2-Pyridyl | PhOCH ₂ | 115-116 (EtOH) | ... | 263 |
| C ₁₆ H ₁₄ NO ₃ Cl | <i>p</i> -ClC ₆ H ₄ | PhOCH ₂ | 158-162 (Me ₂ CO) | ... | 263 |
| C ₁₆ H ₁₄ N ₂ O ₅ | <i>p</i> -O ₂ NC ₆ H ₄ | PhOCH ₂ | 162-163 (Me ₂ CO) | ... | 263, 264 |
| C ₁₆ H ₁₅ NO ₃ | Ph | PhOCH ₂ | 139-140 (Me ₂ CO) | 100 | 263, 264 |
| C ₁₇ H ₁₇ NO ₃ | <i>p</i> -MeC ₆ H ₄ | PhOCH ₂ | 149-151 (Me ₂ CO) | ... | 263 |
| C ₁₈ H ₁₉ NO ₄ | <i>p</i> -EtOC ₆ H ₄ | PhOCH ₂ | 131-133 (Me ₂ CO) | ... | 263 |

Structure

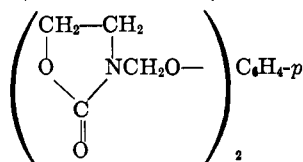


264



185-187

264



206-210

264

^a R₂ = R₃ = R₅ = H.

on this reaction. The reaction is carried out without solvent or catalyst at high temperatures.

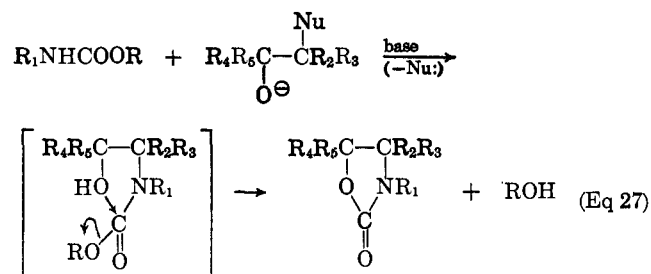
5. Use of Urethans (Table XXI)

Urethan and substituted urethans have also been used to react with epoxides. A small amount of nu-

cleophilic catalyst seems to be necessary, such as potassium hydroxide (44, 323), tertiary amines (263, 328), quaternary ammonium salts (263), and betaine (328).

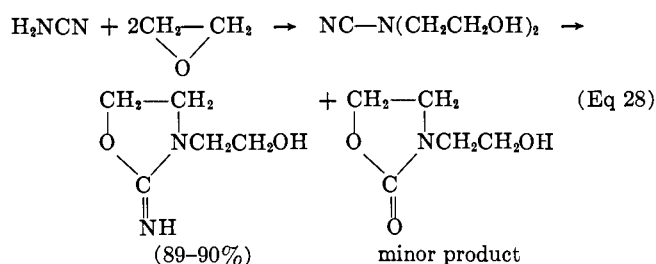
A suggested mechanism (263) requires the catalyst to open the epoxide ring, and the urethan then displaces the nucleophile (Nu) forming an N-(β-hydroxy-

ethyl)urethan which cyclizes with loss of alcohol (Eq 27).



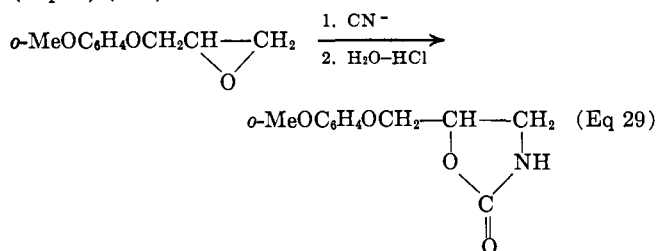
6. Use of Cyanamide

A small amount of 2-oxazolidone is reported to be formed from ethylene oxide and cyanamide (331) (Eq 28). Cyanogen bromide and diethanolamine are claimed to react similarly.



7. Use of Cyanide Ion

An oxazolidone is reported to be produced by reaction of sodium cyanide in ethanol with an epoxide (Eq 29) (323).



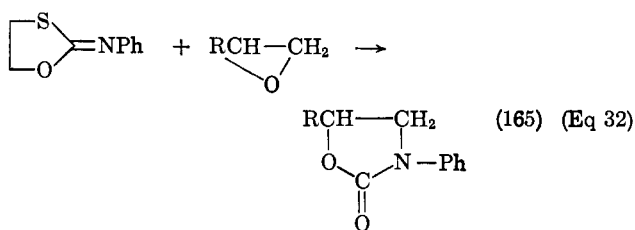
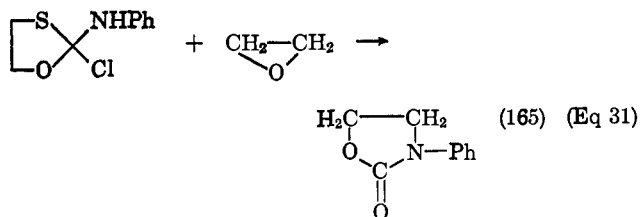
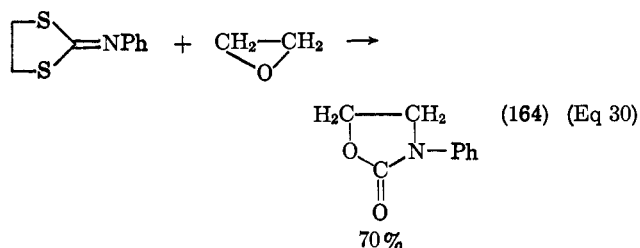
8. Use of Dithiolanes and Oxathiolanes (Table XXII)

Russian workers (164, 165) have reported that five-membered heterocycles containing oxygen and sulfur in various combinations react with epoxides to yield 2-oxazolidones (Eq 30-32). There is no indication of mechanism, and the conditions of the reaction are not clear; in some cases either triethylamine or tetraethylammonium bromide serves as catalyst.

TABLE XXII

2-OXAZOLIDONES PREPARED ACCORDING TO Eq 32

| Empirical formula | R | Mp, °C | % yield | Ref |
|--|-------------------|--------|---------|-----|
| C ₉ H ₉ NO ₂ | H | 120 | 63 | 165 |
| C ₁₀ H ₁₀ NO ₂ Cl | ClCH ₂ | 103 | 51 | 165 |
| C ₁₀ H ₁₁ NO ₂ | Me | 81.5 | 51 | 165 |



I. FROM CYCLIC CARBONATES (2-DIOXOLANONES)

1. Use of Isocyanates (Table XXIII)

In contrast to the reaction of β -amino alcohols with organic carbonates, in which the two-carbon-atom "backbone" of the oxazolidone is supplied by the alcohol, 2-oxazolidones can also be prepared by reaction of a cyclic carbonate with an isocyanate, in which case the "backbone" is supplied by the carbonate. Both inorganic salts, such as lithium chloride (214), zinc chloride, stannous chloride, sodium hydroxide, sodium carbonate, and potassium carbonate (226), and tertiary amines, such as pyridine (216) and N-methylmorpholine (548, 549), have been used as catalysts.

One group of workers (548, 549) has suggested that an intermediate is formed at slightly elevated temperatures (about 70°) reported to be a molecular complex of the isocyanate and the carbonate. This complex can be recrystallized and exhibits a sharp melting point. When heated, it decomposes, carbon dioxide is evolved, and a 2-oxazolidone is formed. When the reaction is carried out in one stage at the higher temperature, no appreciable complex formation is noted.

In a tracer study of the reaction (329), it has been found that approximately 90% of the carbon dioxide evolved comes from the ethylene carbonate and 10% from transformed isocyanate. Accordingly, the mechanism shown in Eq 33a-e has been suggested.

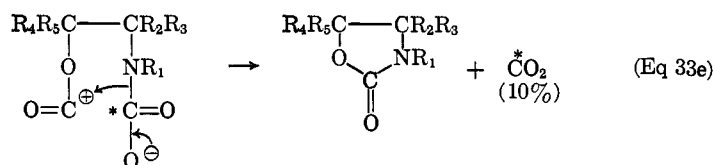
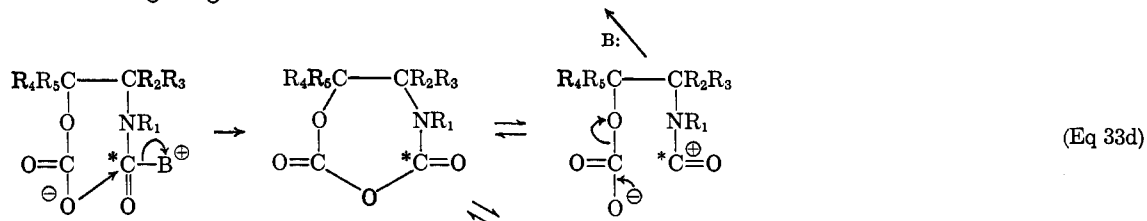
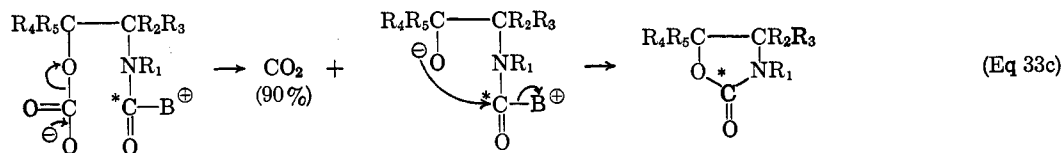
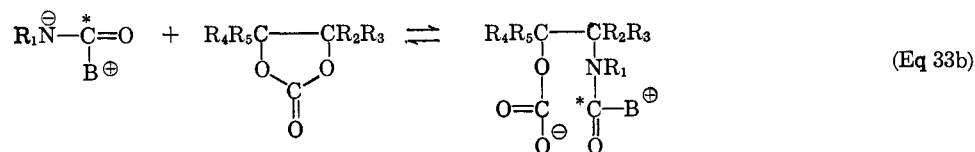
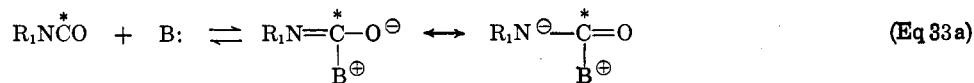
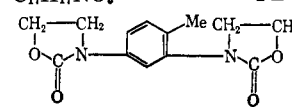


TABLE XXIII

2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES AND ISOCYANATES

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|--|--------------------|----------------|----------------------------------|---------|-----------------------|
| C ₇ H ₁₂ NO ₂ | <i>n</i> -C ₄ H ₉ | H | H | 122-124 (18) | 91 | 216 |
| C ₉ H ₈ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | H | H | 116-117 | 70 | 548, 550 |
| C ₉ H ₉ NO ₂ | Ph | H | H | 117-119 (EtOH), 121-122, 196 (2) | 92 | 214-216, 226, 548-550 |
| C ₉ H ₁₆ NO ₂ | Cyclohexyl | H | H | 33-33.4 | 95 | 214, 215 |
| C ₁₄ H ₁₁ NO ₂ | <i>p</i> -MeC ₆ H ₄ | H | H | 90 | 63 | 548, 550 |
| | PhCH ₂ | H | H | 79-80 | 30 | 214 |
| | Ph | H | Me | 79-81, 81-82, 141-142 (0.4) | 94 | 214, 216, 548 |
| C ₁₄ H ₁₇ NO ₂ | Cyclohexyl | H | Me | 39-40 | 96 | 214 |
| C ₁₁ H ₁₃ NO ₂ | PhCH ₂ | H | Me | 122-124 (0.2) | 26 | 214 |
| C ₁₁ H ₁₃ NO ₃ | <i>p</i> -EtOC ₆ H ₄ | H | H | 95-96 | 78 | 548 |
| C ₁₂ H ₁₃ NO ₄ | <i>p</i> -EtOCOC ₆ H ₄ | H | H | 109.5 | 98 | 214, 215 |
| C ₁₃ H ₁₅ NO ₄ | <i>p</i> -EtOCOC ₆ H ₄ | H | Me | 97-98 | 91 | 214, 215 |
| C ₁₅ H ₂₉ NO ₂ | <i>n</i> -C ₁₂ H ₂₅ | H | H | 167-168 (0.25) | 54 | 214 |
| C ₁₆ H ₃₁ NO ₂ | <i>n</i> -C ₁₂ H ₂₅ | H | Me | 36-37 | 48 | 214 |
| C ₁₇ H ₁₇ NO ₃ | Ph | PhOCH ₂ | H | 137-138, 233-234 (0.5) | 88 | 215, 216 |
|  | | | | Syrupy | .. | 550 |

^a R₃ = R₅ = H.

2. Use of Formamide (Table XXIV)

2-Oxazolidones have been prepared by refluxing cyclic carbonates with formamide (456). Carbon dioxide is eliminated. The mechanism is unclear (Eq 34); in all cases a methylene group is attached to one carbon atom of the carbonate "backbone." The

methylene group is converted into a methyl group.

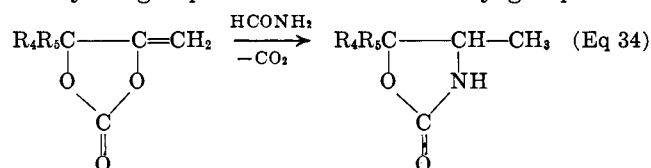


TABLE XXIV
2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES
AND FORMAMIDE

| Empirical formula ^a | R ₁ | R ₂ | Bp (mm) or mp, °C | Ref |
|---|------------------------------------|----------------|--|-----|
| C ₆ H ₁₁ N ₂ O ₂ | Me | Me | 60–62 (Et ₂ O–pet. ether), 114–119 (0.1) | 456 |
| C ₇ H ₁₃ N ₂ O ₂ | Me | Et | 129–130 (0.3) | 456 |
| C ₉ H ₁₅ N ₂ O ₂ | –(CH ₂) ₅ – | | 110–111 (EtOAc), 155– 167 (0.1) | 456 |
| C ₉ H ₁₉ N ₂ O ₂ | Me | <i>i</i> -Bu | 39–41 (pet. ether), 139– 146 (0.1) | 456 |
| C ₁₁ H ₁₉ N ₂ O ₂ | –(CH ₂) ₇ – | | 108 (0.25) | 456 |

^a R₁ = R₂ = H; R₃ = CH₃.

3. Use of Ammonium Carbonate and
Potassium Cyanide (Table XXV)

The preparation of 2-oxazolidones in high yields by reaction of cyclic carbonates with ammonium carbonate and potassium cyanide at 80° has been reported (457, 458).

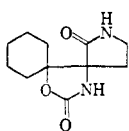
J. FROM ACETYLENIC COMPOUNDS

1. Acetylenic Alcohols plus Isocyanates (Table XXVI)

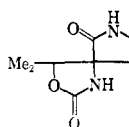
Acetylenic alcohols react with isocyanates to form substituted 4-methylene-2-oxazolidones (Eq 35). Cycli-

TABLE XXV
2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES AND AMMONIUM CARBONATE AND POTASSIUM CYANIDE

| Empirical formula ^a | R ₂ | R ₃ | R ₄ | R ₅ | Mp, °C | Ref |
|---|--------------------|--|----------------|--|--------------------------------|-----|
| C ₇ H ₁₀ N ₂ O ₂ | NC | Me | Me | Me | 106–107 (EtOAc–pet. ether) | 458 |
| C ₇ H ₁₀ N ₂ O ₂ | NC | HOCH ₂ | Me | Me | 110–112 | 458 |
| C ₇ H ₁₂ N ₂ O ₂ | H ₂ NCO | Me | Me | Me | 207–209 (H ₂ O) | 457 |
| C ₈ H ₁₀ N ₂ O ₂ | NC | Me | Me | OHCH ₂ | ... | 458 |
| C ₈ H ₁₀ N ₂ O ₂ | NC | Me | Me | MeOCO | 135–137 | 458 |
| C ₈ H ₁₂ N ₂ O ₂ | NC | Me | Me | Et | 88–89 | 458 |
| C ₈ H ₁₂ N ₂ O ₂ | NC | Me | Me | MeOCH ₂ | ... | 458 |
| C ₈ H ₁₄ N ₂ O ₂ | H ₂ NCO | Me | Me | Me | 135–136 | 458 |
| C ₈ H ₁₄ N ₂ O ₂ | H ₂ NCO | Me | Me | Et | 224–226 (EtOH) | 457 |
| C ₈ H ₁₄ N ₂ O ₂ | H ₂ NCO | Me | Me | MeOCH ₂ | 205–206 (MeOH) | 457 |
| C ₈ H ₁₆ N ₂ O ₂ | H ₂ NCO | Me | Me | <i>i</i> -Pr | 192–194 (EtOH) | 457 |
| C ₈ H ₁₆ N ₂ O ₂ | H ₂ NCO | Me | Me | Me ₂ C(OH) | 189–191 (aq HOAc) | 457 |
| C ₁₀ H ₁₄ N ₂ O ₂ | NC | Me | | –(CH ₂) ₅ – | 133–134 | 458 |
| C ₁₀ H ₁₄ N ₂ O ₂ | NC | HOCH ₂ | | –(CH ₂) ₅ – | 240–249 | 458 |
| C ₁₀ H ₁₆ N ₂ O ₂ | NC | Me | Me | <i>i</i> -Bu | 80–83 | 458 |
| C ₁₀ H ₁₆ N ₂ O ₂ | H ₂ NCO | Me | | –(CH ₂) ₅ – | 253–254 (HOAc) | 457 |
| C ₁₁ H ₁₂ N ₂ O ₂ | NC | Me | Me | α -Pyridyl | 143–144.5 | 458 |
| C ₁₁ H ₁₄ N ₂ O ₂ | NC | Me ₂ C(OH)C≡C | Me | Me | 210–211 | 458 |
| C ₁₁ H ₁₆ N ₂ O ₂ | NC | MeOCH ₂ | | –(CH ₂) ₅ – | 152–153 | 458 |
| C ₁₁ H ₁₉ N ₂ O ₂ | NC | Et ₂ NCH ₂ | Me | Me | ... | 458 |
| C ₁₂ H ₁₂ N ₂ O ₂ | NC | Me | Me | Ph | 139.5–140.5 | 458 |
| C ₁₂ H ₁₄ N ₂ O ₂ | H ₂ NCO | Me | Me | Ph | 217–219 (malonic ester) | 457 |
| C ₁₂ H ₁₈ N ₂ O ₂ | NC | Me | | –(CH ₂) ₇ – | 106.5–107.5 | 458 |
| C ₁₂ H ₁₈ N ₂ O ₂ | NC | Me | Me | 3-Methyl-3-pentenyl | 82–83 | 458 |
| C ₁₂ H ₁₈ N ₂ O ₂ | H ₂ NCO | Me ₂ C(OH)C≡CCH ₂ | Me | Me | 211–213 (DMF–H ₂ O) | 458 |
| C ₁₃ H ₁₄ N ₂ O ₂ | NC | PhCH ₂ | Me | Me | 149 | 457 |
| C ₁₃ H ₁₆ N ₂ O ₂ | H ₂ NCO | PhCH ₂ | Me | Me | 226–227 (THF–pet. ether) | 457 |
| C ₁₃ H ₁₈ N ₂ O ₂ | NC | CH ₂ =CH(CH ₂) ₂ | | –(CH ₂) ₅ – | 133.5–135.5 | 458 |
| C ₁₃ H ₂₂ N ₂ O ₂ | NC | Me | Me | Et ₂ N(CH ₂) ₃ | Oil | 458 |
| C ₁₃ H ₂₃ N ₂ O ₂ | NC | β -(N-Morpholino)ethyl | | –(CH ₂) ₅ – | 133–134 | 458 |
| C ₁₃ H ₂₅ N ₂ O ₂ | H ₂ NCO | Me | Me | Et ₂ N(CH ₂) ₃ | 164–165 (THF–pet. ether) | 457 |
| C ₁₆ H ₂₆ N ₂ O ₂ | NC | Me | | –(CH ₂) ₁₁ – | 156–158 | 458 |
| C ₁₆ H ₂₈ N ₂ O ₂ | H ₂ NCO | Me | | –(CH ₂) ₁₁ – | 258–260 (N-methylpyrrolidone) | 457 |
| C ₁₇ H ₂₆ N ₂ O ₂ | NC | Me | Me | 4,8-Dimethyl-3,7-nonadienyl | ... | 458 |
| C ₂₂ H ₄₀ N ₂ O ₂ | NC | Me | Me | 4,8,12-Trimethyl-tridecyl | ... | 458 |



283 dec (malonic ester–HOAc) 457

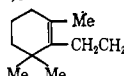
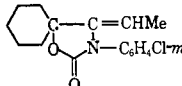


281–285 dec (HOAc–MeOH) 457

^a R₁ = H.

TABLE XXVI

4-METHYLENE-2-OXAZOLIDONES PREPARED FROM ACETYLENIC ALCOHOLS AND ISOCYANATES

| Empirical formula ^a | R ₁ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|------------------------------------|---|---|---------|-------------------|
| C ₈ H ₁₃ NO ₂ | Et | Me | Me | 72-74 (0.3-0.6) | 70 | 471 |
| C ₉ H ₁₅ NO ₂ | Et | Me | Et | 87-91 (1.2-1.5) | 60 | 471 |
| C ₁₀ H ₇ NO ₂ Cl ₂ | 3,4-Cl ₂ C ₆ H ₃ | H | H | 152-153 | 93 | 504 |
| C ₁₀ H ₉ NO ₂ | Ph | H | H | 94-97 (CHCl ₃ -isooctane); 97.2-97.7 (MeOH), 97.5-98.0 | 96 | 83, 471, 503, 504 |
| C ₁₂ H ₁₁ NO ₂ Cl ₂ | 3,4-Cl ₂ C ₆ H ₃ | Me | Me | 134.2-135.1, 140.2-140.8 | 63 | 83, 504 |
| C ₁₂ H ₁₂ NO ₂ Cl | <i>m</i> -ClC ₆ H ₄ | Me | Me | 102.0-102.5 | .. | 83 |
| C ₁₂ H ₁₃ NO ₂ Cl | Ph | Me | Me | 130-133 (EtOH), 131.5-132.0 | 90 | 83, 471 |
| C ₁₃ H ₁₃ NO ₂ Cl | 3,4-Cl ₂ C ₆ H ₃ | Et | Me | 87-89 (pet. ether), 88.1-88.9 | 90 | 471, 504 |
| | 2,5-Cl ₂ C ₆ H ₃ | Me | Et | 134-135 (1,2-dimethoxyethane) | 50 | 471 |
| | 3,4-Cl ₂ C ₆ H ₃ | Me | Et | 88.6-88.8 | .. | 83 |
| C ₁₃ H ₁₄ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | Me | Et | 112-119 (Et ₂ O) | 60 | 471 |
| C ₁₆ H ₁₅ NO ₂ Cl ₂ | 3,4-Cl ₂ C ₆ H ₃ | -(CH ₂) ₅ - | | 161.5-162.1 | 67 | 504 |
| C ₁₅ H ₁₆ NO ₂ Cl | <i>m</i> -ClC ₆ H ₄ | -(CH ₂) ₅ - | | 142-143 | 89 | 504 |
| C ₁₅ H ₁₇ NO ₂ | Ph | -(CH ₂) ₅ - | | 166-168 (EtOH), 167.1-167.6 (pet. ether), 168.9-170.0 | 89 | 83, 471, 477, 504 |
| C ₂₂ H ₂₉ NO ₂ | Ph | Me |  | 129-130 (pet. ether) | .. | 477 |
| | | |  | 150.8-151.6 (hexane) | .. | 83 |

^a R₂R₃ = methylene.

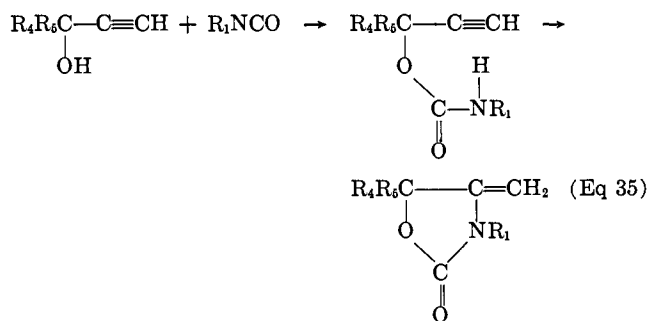
TABLE XXVII

4-ALKYL-2-OXAZOLIDONES PREPARED FROM 4-ALKYLIDENE-2-OXAZOLIDONES BY CATALYTIC HYDROGENATION

| Empirical formula ^a | R ₁ | R ₂ | Mp, °C | % yield | Ref |
|--|---|----------------|----------------------------|---------|-----|
| C ₁₀ H ₉ NO ₂ Cl ₂ | 3,4-Cl ₂ C ₆ H ₃ | Me | 88.7-89.5 (MeOH) | 73 | 504 |
| C ₁₀ H ₁₁ NO ₂ | Ph | Me | 49-50° (Et ₂ O) | 66 | 504 |

^a R₃ = R₄ = R₅ = H.

zation is effected by bases, such as sodium methoxide (471) and pyridine (83), or merely by heating (504). Pyridine is a convenient solvent for the reaction.

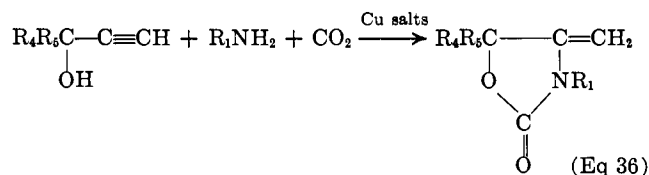


Hydrogenation of 4-alkylidene-2-oxazolidones using palladium on carbon as catalyst yields 4-alkyl-2-oxazolidones (504) (Table XXVII).

2. Acetylenic Alcohols Plus Amines and Carbon Dioxide (Table XXVIII)

5,5-Disubstituted 4-methylene-2-oxazolidones are obtained by the reaction of acetylenic alcohols with amines and carbon dioxide at elevated temperatures

and pressures in the presence of catalytic amounts of copper salts (133) (Eq 36).



3. Acetylenic Amines And Carbon Dioxide (Table XXIX)

4,4-Disubstituted 5-methylene-2-oxazolidones are obtained by the reaction of carbon dioxide with acetylenic amines at elevated pressures and temperatures in the presence of copper salts (131) (Eq 37). Tetrahydrofuran is the solvent of choice; catalytic quantities of tertiary amines increase the yield of oxazolidone.

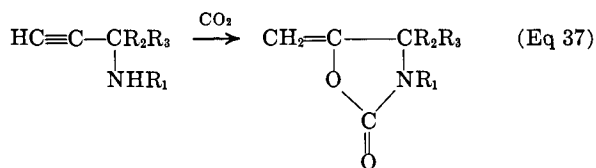


TABLE XXVIII

5,5-DISUBSTITUTED 4-METHYLENE-2-OXAZOLIDONES PREPARED FROM ACETYLENIC ALCOHOLS PLUS AMINES AND CARBON DIOXIDE (133)

| Empirical formula ^a | R ₁ | R ₄ | R ₃ | Bp (mm) or mp, °C |
|---|-----------------------------------|------------------------------------|----------------|------------------------------|
| C ₇ H ₁₁ NO ₂ | Me | Me | Me | 94 (15) |
| C ₈ H ₁₃ NO ₂ | HOCH ₂ CH ₂ | Me | Me | 71-73 (EtOAc), 128-130 (0.6) |
| C ₉ H ₁₅ NO ₂ | <i>i</i> -Pr | Me | Me | 66-69, 110-114 (21) |
| C ₁₀ H ₁₆ NO ₂ | Me | -(CH ₂) ₅ - | | 58-60, 118-120 (1) |
| C ₁₀ H ₁₇ NO ₂ | <i>n</i> -Bu | Me | Me | ... |
| C ₁₁ H ₇ NO ₂ | CH ₂ =C(Me)CH(Me) | Me | Me | 88-90 (0.3) |
| C ₁₁ H ₁₉ NO ₂ | <i>n</i> -Bu | Me | Et | 89-93 (0.5) |
| C ₁₇ H ₁₉ NO ₂ | <i>i</i> -Pr | -(CH ₂) ₅ - | | 89, 138-141 (1) |
| | Cyclohexyl | Me | Me | 68, 140 (0.6) |
| C ₁₃ H ₁₆ NO ₂ | PhCH ₂ | Me | Me | 32-34, 118-121 (0.9) |
| C ₁₃ H ₁₁ NO ₂ | <i>n</i> -Bu | -(CH ₂) ₅ - | | 36-38, 118 (0.3) |
| C ₁₆ H ₁₉ NO ₂ | PhCH ₂ | -(CH ₂) ₅ - | | 79-80 (HOAc) |
| | | | | 115-117 (HOAc) |
| | | | | 86-91 (THF-pet. ether) |

^a R₂R₃ = methylene.

TABLE XXIX

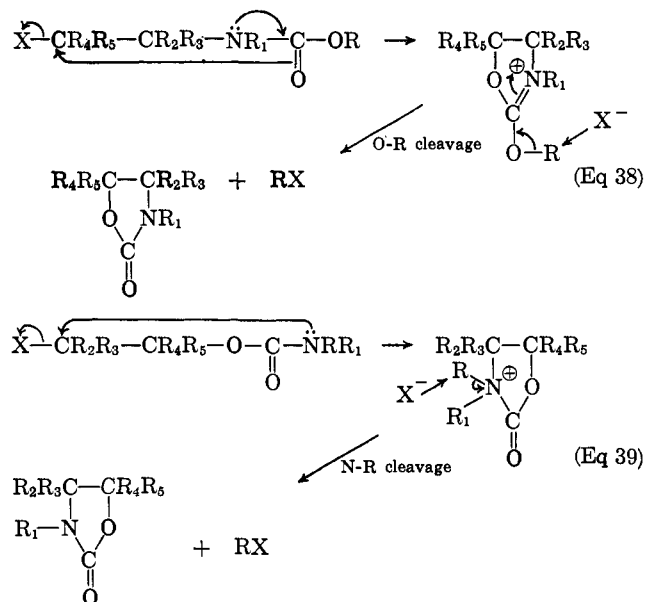
4,4-DISUBSTITUTED 5-METHYLENE-2-OXAZOLIDONES PREPARED FROM ACETYLENIC AMINES AND CARBON DIOXIDE (131)

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Bp (mm) or mp, °C |
|---|-------------------|------------------------------------|----------------|-------------------|
| C ₈ H ₁₃ NO ₂ | <i>i</i> -Pr | Me | H | 67 (0.3) |
| C ₉ H ₁₅ NO ₂ | H | -(CH ₂) ₅ - | | 112 |
| C ₉ H ₁₆ NO ₂ | <i>i</i> -Pr | Me | Me | 125-127 (EtOAc) |
| C ₁₀ H ₁₇ NO ₂ | <i>n</i> -Bu | Me | Me | 102 (1.5) |
| C ₁₁ H ₁₁ NO ₂ | PhCH ₂ | H | H | 37 |
| C ₁₁ H ₁₇ NO ₂ | Et | -(CH ₂) ₅ - | | 110 (0.01) |
| C ₁₃ H ₂₁ NO ₂ | <i>n</i> -Bu | -(CH ₂) ₅ - | | 130 (0.15) |

^a R₄R₅ = methylene.

K. FROM URETHANS

The cyclization of appropriately substituted urethans to form 2-oxazolidones has received much study, presumably because the already existing sequence of nitrogen-carbonyl carbon-oxygen linkages is suitably set up for ring closure. The large number of reported cyclizations can be divided into those carried out (a) pyrolytically without catalysts, (b) with alkaline catalysts, and (c) with acid catalysts. In the ring closures, either the carbonyl oxygen or the nitrogen serves as the nucleophilic species for displacement (Eq 38 or 39, respectively). In Eq 38 the displacement of X occurs on the carbon atom β to the urethan linkage with oxygen-alkyl cleavage. In Eq 39 the displacement occurs with nitrogen-alkyl cleavage (normally either R or R₁ = H), and alkaline catalysts are usually present. A mechanism involving intermediate carbonium ions



has also been suggested (341) but does not appear as likely as the ones suggested.

1. Pyrolytic Cyclizations (Table XXX)

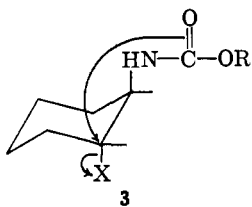
If X (Eq 38 and 39) is sufficiently labile, merely heating the urethan brings about cyclization. Only one case is reported of nitrogen-alkyl cleavage among the purely pyrolytic cyclizations (42). When oxygen-alkyl cleavage occurs, X can be iodine (140), bromine (297), chlorine (286, 368), or even the amino group (142). In oxy-

TABLE XXX
 2-OXAZOLIDONES PREPARED BY PYROLYSIS OF β -SUBSTITUTED URETHANS

| Empirical Formula ^a | R ₁ | R ₂ | R ₃ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|----------------|----------------|----------------|------------------------------------|--|---------|-----------------|
| C ₃ H ₅ NO ₂ | H | H | H | H | ... | 50 | 543 |
| C ₄ H ₇ NO ₂ Cl | H | H | H | ClCH ₂ | 105-106 (H ₂ O) | 80 | 286 |
| C ₄ H ₇ NO ₂ | H | H | H | Me | 109-111 (2), 136-137 (5) | 90 | 286, 368, 543 |
| C ₅ H ₉ NO ₂ Br | H | Me | H | H | 155-160 (11) | Poor | 368 |
| | H | H | H | BrCH ₂ CH ₂ | 107 (C ₆ H ₆) | 70 | 286 |
| C ₅ H ₉ NO ₂ | Me | H | H | BrCH ₂ | 180-190 | ... | 13 |
| | H | H | H | Et | 109 (0.15) | 90 | 543 |
| C ₆ H ₁₀ NO ₂ Cl | H | Et | H | H | ... | Poor | 368 |
| | H | Me | Me | H | 152-154 | ... | 286 |
| | Et | H | H | ClCH ₂ | ... | ... | 13 |
| C ₇ H ₁₁ NO ₂ | H | H | | -(CH ₂) ₄ - | <i>trans</i> , 100-102 (CHCl ₃ -pet. ether); <i>cis</i> , 55-56 (Et ₂ O-pet. ether) | ... | 358 230, 358 |
| C ₈ H ₁₃ NO ₂ | Me | H | | -(CH ₂) ₄ - | <i>trans</i> , 51-52 (EtOAc-pet. ether); | ... | 358 |
| | | | | | <i>cis</i> , 110-115 (0.02) | ... | 358 |
| C ₉ H ₉ NO ₂ | Ph | H | H | H | ... | 95 | 42, 286 |
| | H | H | H | Ph | 90-91 (CHCl ₃ -C ₆ H ₆) | 45 | 543 |
| | H | Ph | H | H | 136 | ... | 230 |
| Name | | | | | | | |
| Cholestano[3 β ,2 β -b]-2-oxazolidone | | | | | 227 | | 230 |
| <i>cis</i> -Tetralino[2,1-b]-2-oxazolidone | | | | | 141 | | 230 |
| <i>cis</i> -Indano[2,1-b]-2-oxazolidone | | | | | 160 | | 230 |

^a R₅ = H.

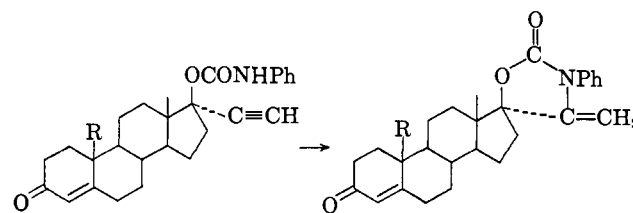
gen-alkyl cleavage, the process is similar to an S_N2 reaction and hence is stereospecific (Eq 38) (230). This can be seen from the perspective diagram 3. In the case of a β -halocyclohexane carbamate in the *trans*-diaxial configuration, rearward attack by carbonyl oxygen on the carbon bearing halogen yields an oxazolidone with a *cis* ring fusion, *cis*-cyclohexano[*b*]-2-oxazolidone.



2. Alkaline Cyclizations (Table XXXI)

Alkaline cyclizations of urethans have received wide attention. As Table XXXI shows, yields are generally fairly good. A variety of bases have been used: alcoholic potassium hydroxide (279, 380, 420, 531), aqueous potassium hydroxide (277, 341), sodium hydroxide (23, 497), sodium ethoxide (116, 119, 120, 122, 123, 367, 395), sodium methoxide (163, 403), trimethylamine (117, 366), triethylamine (492), diethylamine (396), potassium (459), and fused urea (318). Only two groups of workers (318, 359) report alkaline cyclizations *via* oxygen-alkyl cleavage.

There is one example (353) of a cyclization of a urethan under basic conditions involving no loss of a group.



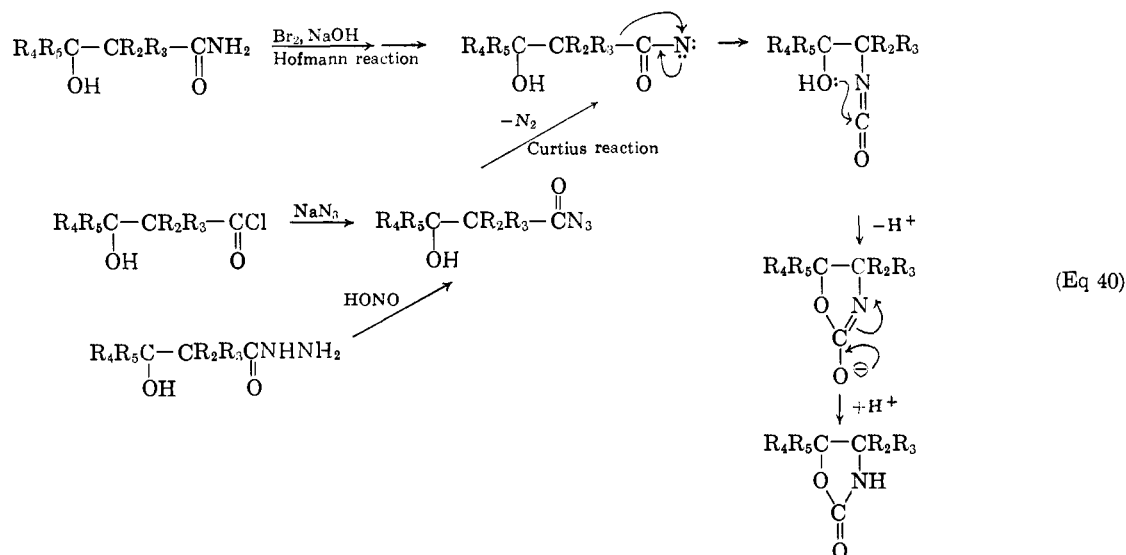
R = Me, mp 281-283°, 84% yield
R = H, mp 269-272°, 74% yield

3. Acidic Cyclizations (Table XXXII)

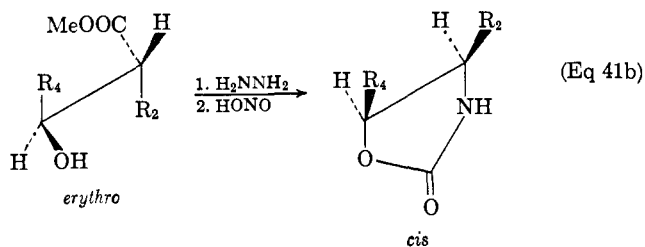
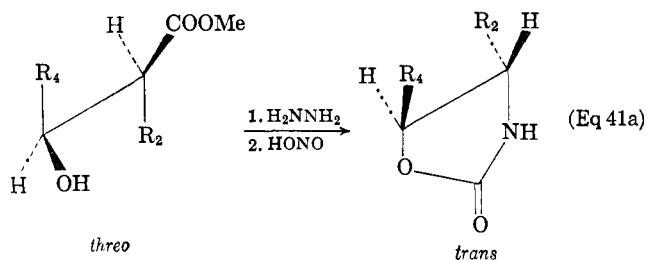
There are only a few cases of cyclizations carried out under acidic conditions. The proton is required to satisfy some structural feature in the molecule and may also be required for initiating the reaction as the starting materials employed are benzylurethans. Both thionyl chloride and phosphorus pentoxide have also been reported as cyclizing reagents in the cyclization of β -hydroxyethyl carbamates (X = OH) (3) (100).

L. FROM β -HYDROXY ISOCYANATES (TABLE XXXIII)

2-Oxazolidones have been prepared from β -hydroxyamides by way of the Hofmann reaction and from β -hydroxyacylazides by way of the Curtius reaction. These two types of reactions are conveniently considered together, as they both proceed through a common intermediate, the isocyanate (171). The production of the oxazolidone can be formulated as in Eq 40.



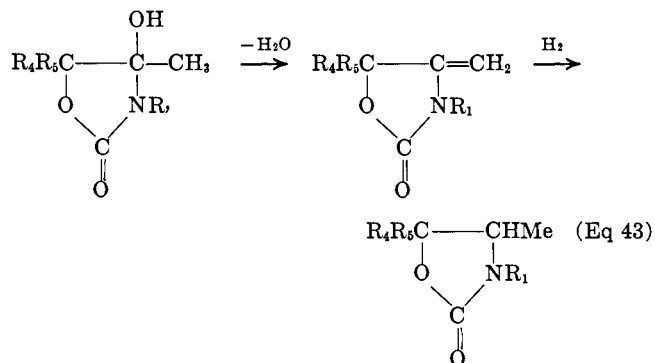
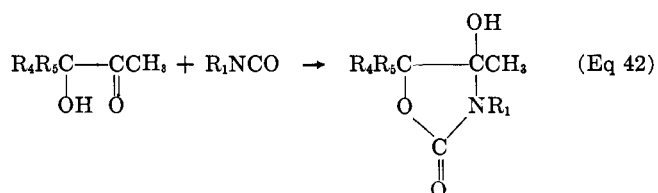
The formation of 2-oxazolidones has been used to prove stereochemical configuration (590, 611) (Eq 41).



M. FROM ACYLOINS (α -KETOLS)

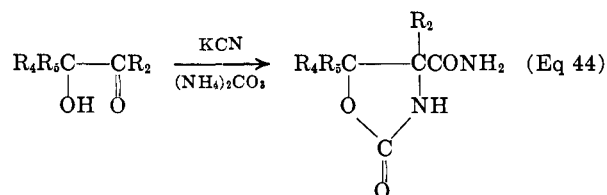
1. Use of Isocyanates (Table XXXIV)

2-Oxazolidones have been prepared by the reaction of isocyanates with acyloins (Eq 42) (148). The product is then dehydrated and catalytically hydrogenated (Eq 43).



2. Use of Potassium Cyanide and Ammonium Carbonate (Table XXXV)

α -Ketols (acyloins) have been converted into 2-oxazolidones by reaction with potassium cyanide and ammonium carbonate (Eq 44) (235). The reaction



product can be hydrolyzed with 4–5 *N* hydrochloric acid to the corresponding carboxylic acid. The acid can either be esterified directly or it can be treated with thionyl chloride followed by methanol to give the corresponding carbomethoxy derivative.

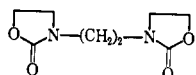
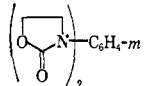
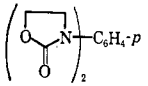
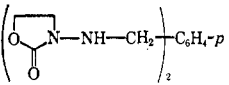
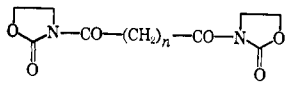
N. FROM NITRENES (TABLE XXXVI)

2-Oxazolidones are reported to be products of the intramolecular insertion of a nitrene into a carbon-hydrogen bond (Eq 45) (482). The nitrenes are produced by pyrolysis or photolysis of an azide; the reaction is reported to go in 45–75% yields.

TABLE XXXI
 2-OXAZOLIDONES PREPARED BY ALKALINE-CATALYZED CYCLIZATION OF URETHANS

| Empirical formula ^a | R ₁ | R ₂ | R ₃ | Bp (mm) or mp, °C | % yield | Ref |
|--|--|-------------------|---|--|---------|---------------|
| C ₅ H ₅ NO ₂ | H | H | H | 90 | ... | 459 |
| C ₅ H ₆ N ₂ O ₂ | H ₂ N | H | H | 70 (EtOH), 34 | ... | 119, 170 |
| C ₄ H ₅ NO ₄ | H | HOOC | H | 118 | ... | 448 |
| C ₄ H ₇ NO ₂ | Me | H | H | 71 (HCl salt) | ... | 123 |
| | Me | H | H | 208 dec (MeCl salt) | ... | 123 |
| | H | H | Me | 89-90 (0.04) | ... | 367 |
| C ₅ H ₇ NO ₂ | CH ₂ =CH | H | H | 100-105 (1.3) | ... | 23 |
| C ₅ H ₈ NO ₂ Cl | ClCH ₂ CH ₂ | H | H | 122-124 (1) | 72 | 23 |
| C ₅ H ₁₀ N ₂ O ₂ | Me ₂ N | H | H | 72 (Et ₂ O) | 87 | 116 |
| C ₆ H ₉ NO ₂ | CH ₂ =CHCH ₂ | H | H | ... | Poor | 420 |
| C ₆ H ₁₁ NO ₂ | H | H | <i>i</i> -Pr | 113-114 (<i>d</i> form) | ... | 375 |
| C ₇ H ₁₂ NO ₂ | <i>n</i> -Bu | H | H | 122 (4) | 80 | 395 |
| | <i>t</i> -Bu | H | H | 94 (2) | 62 | 395 |
| C ₈ H ₇ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | H | 246-247, 255-256 | 83 | 170, 403, 566 |
| C ₈ H ₁₆ N ₂ O ₂ | Me ₂ N(CH ₂) ₃ | H | H | 117, 177 (hygroscopic) | ... | 120, 122 |
| C ₈ H ₇ NO ₂ Cl | 3,4-Cl ₂ C ₆ H ₃ | H | H | 79 | ... | 380 |
| C ₈ H ₇ N ₂ O ₅ Cl | 2-HO-3-NO ₂ -5-ClC ₆ H ₂ | H | H | ... | ... | 497 |
| C ₈ H ₈ NO ₂ Cl | <i>m</i> -ClC ₆ H ₄ | H | H | 53.0-53.5 | 95 | 279, 341 |
| | <i>p</i> -ClC ₆ H ₄ | H | H | 120.9-121.5, 122.5 | 92 | 279, 341, 395 |
| C ₈ H ₈ NO ₂ Br | <i>o</i> -BrC ₆ H ₄ | H | H | 142-147 (0.01) | 76 | 341 |
| | <i>p</i> -BrC ₆ H ₄ | H | H | 139.8-140.6 | 96 | 341 |
| C ₈ H ₈ NO ₃ Cl | 2-HO,5-ClC ₆ H ₃ | H | H | 186 | ... | 497 |
| C ₈ H ₉ N ₂ O ₄ | <i>p</i> -O ₂ NC ₆ H ₄ | H | H | 154.5 | 95 | 395 |
| | <i>o</i> -O ₂ NC ₆ H ₄ | H | H | 110 | 97 | 395 |
| C ₈ H ₉ NO ₂ | Ph | H | H | 118 (C ₆ H ₆), 121-122 | 95 | 395, 492 |
| C ₈ H ₉ N ₂ O ₃ Cl | 2-HO-3-H ₂ N-5-ClC ₆ H ₂ | H | H | ... | ... | 497 |
| C ₁₀ H ₉ NO ₂ Cl ₂ | <i>p</i> -ClC ₆ H ₄ | H | ClCH ₂ | 126.5 | 93 | 279 |
| C ₁₀ H ₁₀ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | H | Me | 114 | 94 | 279 |
| | Ph | ClCH ₂ | H | 73-78 (ligroin) | ... | 277 |
| | Ph | H | ClCH ₂ | 108 | 95 | 277, 279 |
| C ₁₀ H ₁₀ NO ₃ Cl | H | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | 151 | ... | 36 |
| C ₁₀ H ₁₀ N ₂ O ₂ | PhCH=CN | H | H | 141-143 | ... | 566 |
| C ₁₀ H ₁₁ NO ₂ | PhCH ₂ | H | H | 79.5-80.0 | 96 | 123, 341 |
| | <i>o</i> -MeC ₆ H ₄ | H | H | 125-130 (0.001), 170 (4) | 80 | 341, 395 |
| | <i>m</i> -MeC ₆ H ₄ | H | H | 94.3-95.0 | 78 | 341 |
| | <i>p</i> -MeC ₆ H ₄ | H | H | 90.5-91.0 | 70 | 341, 395 |
| C ₁₀ H ₁₁ NO ₃ | <i>m</i> -MeOC ₆ H ₄ | H | H | 77-77.6 | 72 | 341 |
| | <i>p</i> -MeOC ₆ H ₄ | H | H | 109-110 | 93 | 341 |
| C ₁₀ H ₁₃ N ₂ O ₃ | N-Morpholinopropyl | H | H | 171 (<i>n</i> -BuOH) (hygroscopic) (HCl salt) | ... | 122 |
| C ₁₀ H ₂₀ N ₂ O ₂ | Et ₂ N(CH ₂) ₃ | H | H | ... | ... | 122 |
| C ₁₁ H ₁₁ N ₂ O ₃ Cl | PhNHCO | H | ClCH ₂ | 154-155 (alc) | ... | 276 |
| C ₁₁ H ₁₂ NO ₃ Cl | H | H | 3-Cl-6-MeC ₆ H ₃ OCH ₂ | 104-104.5, 200 (0.1) | ... | 318 |
| C ₁₁ H ₁₃ NO ₂ | <i>p</i> -MeC ₆ H ₄ | H | Me | 67.5 | 93 | 279 |
| C ₁₁ H ₁₃ NO ₃ | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | 125.6-126.5 | ... | 36 |
| | <i>p</i> -EtOC ₆ H ₄ | H | H | 94-95 | 92 | 341 |
| C ₁₁ H ₁₃ NO ₄ | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | 140-144, 220-225 (0.1) | ... | 36, 318 |
| C ₁₂ H ₁₃ NO ₄ | <i>p</i> -EtOCOC ₆ H ₄ | H | H | 110 | 97 | 395 |
| C ₁₂ H ₁₃ N ₂ O ₃ Cl | PhCH ₂ NHCO | H | ClCH ₂ | 131-132 (alc) | ... | 276 |
| C ₁₃ H ₁₁ NO ₂ | α -Naphthyl | H | H | 129.5-130.0 | 86 | 341 |
| C ₁₄ H ₁₃ NO ₂ | β -Naphthyl | H | Me | 134 | 95 | 279 |
| C ₁₄ H ₁₃ NO ₃ | H | H | β -Naphthyloxy-methyl | 193.0-193.6 | ... | 36 |
| C ₁₅ H ₁₂ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | H | Ph | 131 | 96 | 279 |
| C ₁₅ H ₁₃ NO ₂ | Ph | H | Ph | 129 | 97 | 279 |
| C ₁₅ H ₂₀ N ₂ O ₄ | $p\text{-}\left(\text{O} \begin{array}{c} \diagup \text{NCH}_2\text{CH}_2\text{O} \diagdown \end{array} \right)\text{C}_6\text{H}_4$ | H | H | ... | ... | 369 |
| C ₁₅ H ₂₉ NO ₂ | <i>n</i> -C ₁₂ H ₂₅ | H | H | 62 (EtOH) | 52 | 531 |
| C ₁₇ H ₁₆ N ₂ O ₄ | 1-Anthraquinonyl | H | H | 226.5 | 85 | 395 |

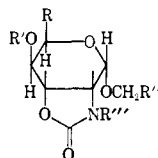
TABLE XXXI (Continued)

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Bp (mm) or mp, °C | % yield | Ref |
|---|---|----------------|------------------------|-------------------|----------------|-----|
| C ₁₇ H ₁₆ N ₂ O ₄ | Ph | H | PhNHCOOCH ₂ | ... | ... | 265 |
| | Structure | | | | | |
| |  | | | 107 | 80 | 395 |
| |  | | | 175 | 62 | 395 |
| |  | | | 253 | 68 | 395 |
| |  | | | 96 (MeOH) | ... | 163 |
| |  | | | n = 0 | 238 (HOAc) | 47 |
| | | | | n = 1 | 169 (HOAc) | 78 |
| | | | | n = 2 | 193.5 (HOAc) | 72 |
| | | | | n = 4 | 138 (HOAc) | 26 |
| | | | | n = 8 | 130-131 (HOAc) | 82 |

^a R₃ = R₅ = H.

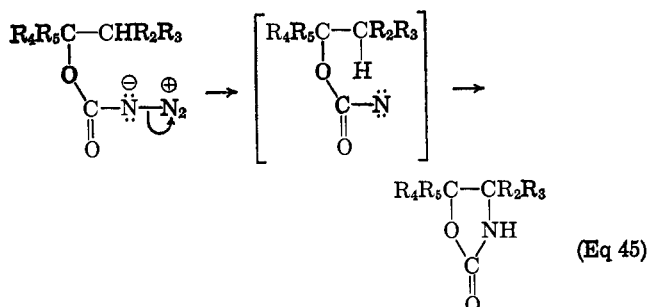
TABLE XXXII

GLUCOPYRANOSIDO-2-OXAZOLIDONES PREPARED BY ACID-CATALYZED CYCLIZATION



| Empirical formula | R | R' | R'' | R''' | Mp, °C | % yield | Ref |
|---|---|--------------------|--------------------|--------------------|------------------------------|---------|-----|
| C ₁₄ H ₁₇ NO ₆ | HOCH ₂ | H | Ph | H | 114 | .. | 210 |
| C ₁₄ H ₁₉ NO ₆ | PhCH ₂ OCH ₂ | H | H | H | 114 (MeOH- <i>i</i> -PrOH) | 90 | 211 |
| C ₁₄ H ₁₈ N ₄ O ₆ | N ₃ CH ₂ | CH ₃ CO | Ph | H | ... | .. | 210 |
| C ₁₇ H ₂₁ NO ₆ S | MeSO ₃ CH ₂ | CH ₃ CO | Ph | H | 177 | .. | 210 |
| C ₁₉ H ₂₃ NO ₆ | PhCH ₂ OCH ₂ | CH ₃ CO | CH ₃ CO | H | 147 (MeOH- <i>i</i> -PrOH) | 80 | 211 |
| C ₂₉ H ₂₅ NO ₆ | PhCH ₂ OCH ₂ | CH ₃ CO | CH ₃ CO | CH ₃ CO | 99-100 (THF- <i>i</i> -PrOH) | 88 | 211 |
| | 3-(5-Nitro-2-furfurylideneamino)-2-oxazolidone ^a | | | | 256-257 dec (DMF) | .. | 100 |

^a Although not a glucopyranoside, this compound is included here because of its method of preparation.



Recent studies have shown that, when the carbon that becomes C-4 in the oxazolidone ring is optically active, the optical activity is retained (482). It is concluded that the cyclization takes place in a one-step process and that the nitrene is in the singlet state, at

least in the case of pyrolytic generation. Another study (600) has confirmed that in the case of a pyrolytically produced nitrene there is 100% retention of configuration in the C-H insertion reaction.

o. FROM (β-HYDROXYALKYL)SEMICARBAZIDES

2-Oxazolidones are obtained by refluxing a solution of a β-hydroxyalkylsemicarbazide with acid (Eq 46) (195, 198). 3-Amino-2-oxazolidone, mp 69-71° (EtOH)

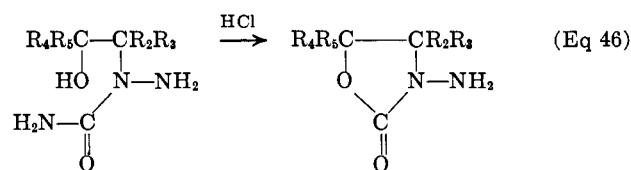




TABLE XXXIII

2-OXAZOLIDONES PREPARED BY WAY OF CURTIUS AND HOFMANN REACTIONS

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|----------------------------|-------------------------|-------------------|---|----------------|---|---------|----------|
| C ₄ H ₇ NO ₃ | H | MeO | H | H | H | ... | .. | 462 |
| C ₆ H ₉ NO ₂ | H | H | H | Me | Me | 56.8-58 (alc-Et ₂ O) | 13 | 97 |
| C ₆ H ₁₁ NO ₂ | H | H | H | <i>i</i> -Pr | H | (<i>l</i>) 113-114 (C ₆ H ₆) | ... | 375, 376 |
| C ₇ H ₁₃ NO ₂ | H | <i>i</i> -Bu | H | H | H | 130-140 (0.2) | 28 | 386 |
| | H | Et | Et | H | H | 160-170 (0.6) | 30 | 386 |
| C ₈ H ₇ N ₃ O ₆ | 5-Nitro-2-furylidene-amino | H | H | H | H | 256-257 (DMF) | 93 | 1, 219 |
| C ₈ H ₁₃ NO ₂ | H | H | H | —(CH ₂) ₆ — | | 101.0-102.4 | 82 | 381 |
| C ₉ H ₉ NO ₂ | H | Ph | H | H | H | 137-139 | 40 | 386 |
| | H | H | H | Ph | H | 89-90 (H ₂ O), 88-90 (alc-Skellysolve B) | 50 | 21, 97 |
| C ₉ H ₁₃ NO ₂ | H | H | H |  | H | 103-104 | 72 | 209 |
| C ₉ H ₁₅ NO ₂ | H | H | H | —(CH ₂) ₄ CHMe— | | 110 | ... | 434 |
| | H | H | H | —(CH ₂) ₂ CHMe(CH ₂) ₂ — | | 131 | ... | 434 |
| | H | H | H | —(CH ₂) ₂ CHMeCH ₂ — | | 118-120 | ... | 434 |
| C ₉ H ₁₅ NO ₃ | H | H | H | —(CH ₂) ₂ CH(OMe)(CH ₂) ₂ — | | 135 | ... | 434 |
| C ₉ H ₁₅ NO ₄ | H | H | H |  | H | ... | ... | 209 |
| C ₁₃ H ₁₀ N ₂ O ₄ | H | PhCONH | H | H | H | 138 | 100 | 463 |
| C ₁₀ H ₁₁ NO ₂ | H | H | H | Ph | Me | 146-147 (EtOH) | 72 | 97 |
| | H | Ph | Me | H | H | 78-79 | 91 | 386 |
| C ₁₀ H ₁₁ NO ₃ | H | H | H | <i>p</i> -MeOC ₆ H ₄ | H | 108-109 (EtOH) | 93 | 55 |
| | H | H | H | <i>m</i> -MeOC ₆ H ₄ | H | 202-203 (BuOH) | 25 | 55 |
| C ₁₀ H ₁₇ NO ₂ | H | H | H | —CH ₂ CHMeCH ₂ CHMeCH ₂ — | | 120 | ... | 434 |
| | H | H | H | —CH ₂ CHMeCHMe(CH ₂) ₂ — | | 103 | ... | 434 |
| | H | H | H | —(CH ₂) ₃ CHEtCH ₂ — | | 109 | ... | 434 |
| | H | H | H | —(CH ₂) ₃ CMe ₂ CH ₂ — | | 148 | ... | 434 |
| | H | H | H | —(CH ₂) ₇ — | | 127 | ... | 434 |
| C ₁₁ H ₁₂ N ₂ O ₂ | PhCH ₂ CH=N | H | H | H | H | 251-256 | ... | 219 |
| C ₁₁ H ₁₂ N ₂ O ₃ | H | PhCH ₂ CONH | H | H | H | (<i>dl</i>) 184 (H ₂ O) | 78 | 37 |
| | | | | | | (<i>d</i>) 157 (H ₂ O) | 77 | 37 |
| | | | | | | (<i>l</i>) 157 (H ₂ O) | 73 | 37 |
| C ₁₁ H ₁₂ N ₂ O ₄ | H | PhCH ₂ OCONH | H | H | H | (<i>dl</i>) 126-127 (MeOH) | 95 | 462 |
| C ₁₁ H ₁₃ NO ₂ | H | Ph | Et | H | H | 80-81 | 89 | 386 |
| C ₁₁ H ₁₃ NO ₃ | H | MeOCH ₂ | H | Ph | H | (<i>dl</i>) <i>cis</i> , 134-135 (C ₆ H ₆ -Et ₂ O) | 60 | 7 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | 2,5-(MeO) ₂ C ₆ H ₃ | H | 107 (C ₆ H ₆) | ... | 41 |
| C ₁₂ H ₁₅ NO ₂ | H | Ph | <i>i</i> -Pr | H | H | 139-140 | 74 | 386 |
| C ₁₂ H ₁₅ NO ₄ | H | H | H | 2,5-(MeO) ₂ C ₆ H ₃ | Me | 159 (C ₆ H ₆) | ... | 41 |
| C ₁₃ H ₁₇ NO ₄ | H | H | H | 2,5-(EtO) ₂ C ₆ H ₃ | H | 86.5 (C ₆ H ₆ -hexane) | ... | 257 |
| C ₁₃ H ₂₁ NO ₂ | H | H | H | <i>trans</i> -2-Decahydro-naphthyl | H | 165 and 200 | ... | 434 |
| | H | H | H | <i>cis</i> -2-Decahydro-naphthyl | H | 140 and 207 | ... | 434 |
| C ₁₅ H ₁₃ NO ₂ | H | H | H | Ph | Ph | 200 (EtOH) | ... | 75 |
| | H | Ph | H | Ph | H | <i>cis</i> , 193.5-194.5; <i>trans</i> , 161-162 | ... | 611 |
| | H | Ph | Ph | H | H | 178-179 | 63 | 386 |
| C ₁₆ H ₁₆ NO ₂ | H | Ph | PhCH ₂ | H | H | 106-107 | 62 | 386 |
| C ₁₆ H ₁₈ NO ₃ | H | H | H | <i>p</i> -PhCH ₂ OC ₆ H ₄ | H | 145-146 (EtOH) | 76 | 55 |
| | H | H | H | <i>m</i> -PhCH ₂ OC ₆ H ₄ | H | 106-107 (EtOH) | 76 | 55 |
| C ₁₇ H ₁₇ NO ₃ | H | H | H | 2-PhCH ₂ O-5-MeC ₆ H ₃ | H | 150-150.5 (C ₆ H ₆ -hexane) | ... | 22 |
| C ₂₁ H ₂₅ NO ₆ | H | H | H | 3,4-(MeO) ₂ C ₆ H ₃ CH ₂ | | 161 (MeOH) | 86 | 472 |
| | | | | 3,4-(MeO) ₂ -C ₆ H ₃ CH ₂ | | (<i>d</i>) 233-235 (MeOH), (<i>l</i>) 244-246 (MeOH) | ... | 505 |

Name
4-Dihydrolysergylamido-2-oxazolidone

TABLE XXXIII (Continued)

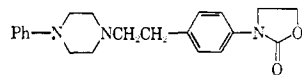

| Name or structure | Bp (mm) or mp, °C | % yield | Ref |
|---|--|--|--|
| 4-Dihydrolysergylamido-5,5-dimethyl-2-oxazolidone | (d) 268-270 (Me ₂ CO), (l) 280 (MeOH) | ... | 505 |
|  | 194-196 | 14 | 333 |
|  | R = 8-Hydroxy-6-sulfonaphth-2-yl 7-Hydroxynaphth-1-yl 5-Hydroxy-7-sulfonaphth-2-yl 6-Hydroxy-8-sulfonaphth-2-yl 5-Hydroxy-1,7-disulfonaphth-2-yl 8-Hydroxy-3,6-disulfonaphth-2-yl | | 498 498 498 498 498 498 |

TABLE XXXIV

2-OXAZOLIDONES PREPARED FROM ISOCYANATES AND ACYLOINS (148)

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Mp, °C | % yield |
|--|---|--------------------|----------------|----------------|----------------|-------------------------------|---------|
| C ₁₂ H ₁₂ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | —CH ₂ — | | Me | Me | 98-99 (MeOH) | 65 |
| C ₁₂ H ₁₃ NO ₂ | Ph | —CH ₂ — | | Me | Me | 94-95 (pet. ether, then EtOH) | 68 |
| C ₁₂ H ₁₄ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | Me | H | Me | Me | ... | .. |
| C ₁₂ H ₁₄ NO ₃ Cl | <i>p</i> -ClC ₆ H ₄ | Me | HO | Me | Me | ... | .. |
| C ₁₂ H ₁₅ NO ₂ | Ph | Me | H | Me | Me | 98-99 (MeOH) | 86 |
| C ₁₂ H ₁₅ NO ₃ | Ph | Me | HO | Me | Me | ... | .. |
| C ₁₈ H ₁₄ NO ₂ Cl | <i>p</i> -ClC ₆ H ₄ | —CH ₂ — | | Et | Me | ... | .. |

TABLE XXXV

2-OXAZOLIDONES PREPARED FROM ACYLOINS AND POTASSIUM CYANIDE PLUS AMMONIUM CARBONATE (235)

| Empirical formula ^a | R ₃ | R ₄ | R ₅ | Mp, °C | % yield |
|---|--------------------|----------------|------------------------------------|----------------------|---------|
| C ₇ H ₁₁ NO ₄ | HOCO | Me | Me | 206-207 | 74 |
| C ₇ H ₁₂ N ₂ O ₃ | H ₂ NCO | Me | Me | 208-209 | 34 |
| C ₈ H ₁₃ NO ₄ | HOCO | Me | Et | 206-207 | 80 |
| | MeOCO | Me | Me | 99-100 | 58 |
| C ₈ H ₁₄ N ₂ O ₃ | H ₂ NCO | Me | Et | 224-226 | 31 |
| C ₉ H ₁₅ NO ₄ | HOCO | Et | Et | 177-179 | 66 |
| C ₉ H ₁₆ N ₂ O ₃ | H ₂ NCO | Et | Et | 175-177 | 72 |
| C ₁₀ H ₁₅ NO ₄ | HOCO | | —(CH ₂) ₅ — | 205-206 | 73 |
| C ₁₀ H ₁₆ N ₂ O ₃ | H ₂ NCO | | —(CH ₂) ₅ — | 253-254 | 79 |
| C ₁₀ H ₁₇ NO ₄ | HOCO | Me | <i>i</i> -Bu | 186-187 ^b | 74 |
| | HOCO | Me | <i>i</i> -Bu | 195-196 ^b | 69 |
| C ₁₀ H ₁₈ N ₂ O ₃ | H ₂ NCO | Me | <i>i</i> -Bu | 192-194 ^b | 39 |
| | H ₂ NCO | Me | <i>i</i> -Bu | 176-178 ^b | 19 |
| C ₁₁ H ₁₇ NO ₄ | MeOCO | | —(CH ₂) ₅ — | 129-131 | 33 |
| C ₁₁ H ₁₉ NO ₄ | MeOCO | Me | <i>i</i> -Bu | 89-90 | 69 |
| C ₁₂ H ₁₈ NO ₄ | HOCO | Me | Ph | 198-199 | 72 |
| C ₁₂ H ₁₄ N ₂ O ₃ | H ₂ NCO | Me | Ph | 222-224 | 24 |

^a R₁ = H; R₂ = Me. ^b Diastereoisomers.

TABLE XXXVI

2-OXAZOLIDONES BY INTRAMOLECULAR INSERTION OF NITRENES INTO A CARBON-HYDROGEN BOND

| Empirical formula ^a | R ₂ | R ₃ | R ₄ | R ₅ | Mp, °C | % yield | Ref |
|--|----------------|----------------|----------------|----------------|--------|---------|---------------|
| C ₃ H ₅ NO ₂ | H | H | H | H | ... | .. | 296 |
| C ₄ H ₇ NO ₂ | H | H | Me | H | ... | .. | 296 |
| C ₆ H ₉ NO ₂ | H | H | Me | Me | 80-81 | 75 | 295, 296, 431 |
| C ₆ H ₁₁ NO ₂ | Et | Me | H | H | ... | 68 | 482, 600 |

^a R₁ = H.

TABLE XXXVII
 2-OXAZOLIDONES FROM 2-OXAZOLINES AND WATER

| Empirical formula ^a | R ₂ | R ₃ | R ₄ | Mp, °C | % yield | Ref |
|--|---|----------------|----------------|----------------------------|---------|----------|
| C ₁₃ H ₁₂ NO ₄ Cl | <i>p</i> -ClC ₆ H ₄ COOCH ₂ | Me | H | 117 | .. | 441, 442 |
| C ₁₂ H ₁₅ NO ₄ | <i>p</i> -MeC ₆ H ₄ COOCH ₂ | Me | H | 169 (H ₂ O) | .. | 441, 442 |
| C ₁₂ H ₁₅ NO ₅ | <i>p</i> -MeOC ₆ H ₄ COOCH ₂ | Me | H | 86 (H ₂ O) | .. | 441 |
| C ₁₆ H ₁₉ NO ₅ | 3,4,5-(MeO) ₃ C ₆ H ₂ COOCH ₂ | Me | H | 144-145 (H ₂ O) | .. | 441, 442 |
| C ₁₇ H ₁₅ NO ₄ | PhCOOCH ₂ | H | Ph | 87-87.5 (EtOH-hexane) | 4 | 426 |

^a R₁ = R₅ = H.

 TABLE XXXVIII
 2-OXAZOLIDONES FROM 2-IMINOXAZOLIDINES

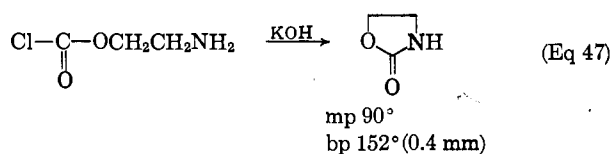
| Empirical formula ^a | R ₁ | R ₂ | R ₄ | Mp, °C | Ref |
|--|---|----------------|------------------------------------|------------|-----|
| C ₈ H ₇ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | H | 253-256 | 154 |
| C ₉ H ₉ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | Me | 245-248 | 154 |
| | 5-Nitro-2-furfurylideneamino | Me | H | 199-200 | 154 |
| C ₁₀ H ₉ N ₃ O ₅ | 3-(5-Nitro-2-furyl)acrylideneamino | H | H | 270 | 154 |
| C ₁₁ H ₁₂ N ₂ O ₂ S | PhNHCS | H | Me | 114 (EtOH) | 183 |
| C ₁₁ H ₁₂ N ₂ O ₅ S | <i>p</i> -MeCONHC ₆ H ₄ SO ₂ | H | H | 175 | 272 |
| C ₁₁ H ₁₃ NO ₂ | Me | Me | Ph | ... | 176 |
| C ₁₂ H ₁₅ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | Bu | 194 | 154 |
| C ₁₅ H ₁₉ N ₂ O ₂ S ₂ | CH ₂ =CHCH ₂ NHCS | H | PhCH ₂ SCH ₂ | 59 (EtOH) | 183 |
| C ₁₉ H ₂₀ N ₂ O ₂ S ₂ | PhNHCS | H | PhCH ₂ SCH ₂ | 107 (EtOH) | 183 |

^a R₃ = R₅ = H.

(195), and 3-amino-4,4-dimethyl-2-oxazolidone, bp 130-135° (10 mm), are reported to have been prepared in this way.

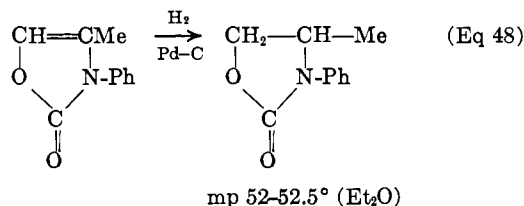
P. FROM β-AMINO CHLOROFORMATES

2-Oxazolidone is obtained by heating an amino chloroformate with aqueous potassium hydroxide (Eq 47) (231). This is the sole example of the reaction.

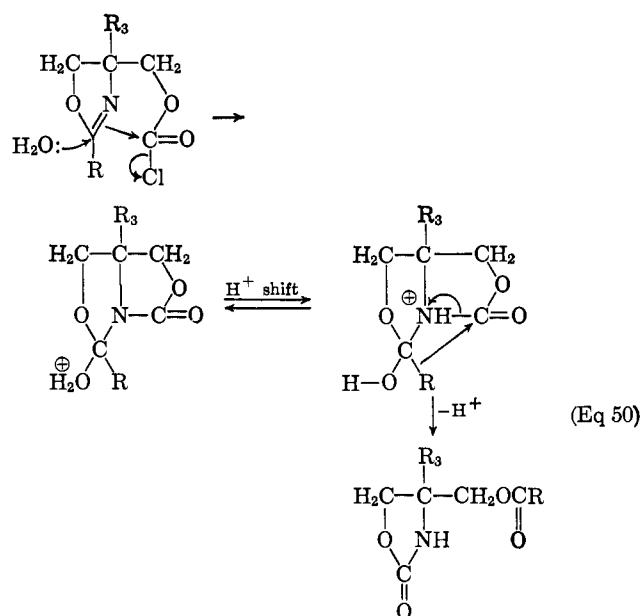
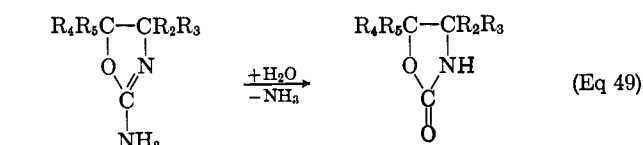


Q. FROM OXAZOLINES AND OXAZOLINONES (TABLE XXXVII)

In one case (477), an oxazolinone was reduced to an oxazolidone with hydrogen at atmospheric pressure and room temperature employing a palladium-on-carbon catalyst (Eq 48).



Another special reaction type is the conversion of 2-amino- or 2-alkyl-2-oxazolines to 2-oxazolidones by refluxing in water (Eq 49 and 50) (426, 441, 442).



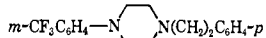
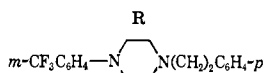
R. FROM 2-IMINOXAZOLIDINES (TABLE XXXVIII)

2-Iminooxazolidines are converted to 2-oxazolidones by hydrolysis with sulfuric or nitrous acid (154, 176) (Eq 51)

TABLE XXXIX
 2-OXAZOLIDONES (MISCELLANEOUS)

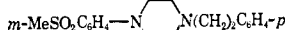
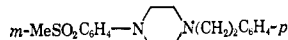
| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Mp, °C | % yield | Ref |
|--|--|----------------|----------------|---|----------------|------------------------------|---------|-----|
| C ₄ H ₇ NO ₂ | H | H | H | Me | H | ... | 90 | 280 |
| C ₅ H ₉ N ₃ O ₂ SCl | 4-Cl-3-(H ₂ NSO ₂)C ₆ H ₄ | H | H | H | H | 182-183 | .. | 280 |
| C ₁₁ H ₁₄ NO ₃ | Me | H | H | <i>m</i> -MeOC ₆ H ₄ | H | Oily | .. | 527 |
| | Me | H | H | <i>p</i> -MeOC ₆ H ₄ | H | 72-75 | .. | 527 |
| C ₁₃ H ₁₆ N ₄ O ₃ | 5-Nitro-2-furfurylidene-amino | H | H | N-Morpholino-methyl | H | 205-206 (Me ₂ CO) | .. | 374 |
| C ₁₃ H ₂₂ N ₂ O ₄ Cl | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₄ CHCl- | | ... | 55 | 434 |
| C ₁₃ H ₂₂ N ₂ O ₄ | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₅ - | | HCl salt, 205 (EtOH) | 72 | 434 |
| C ₁₄ H ₂₀ N ₂ O ₂ | Me ₂ NCH ₂ CH ₂ | Me | H | Ph | H | (<i>cis</i>) | 57 | 609 |
| | | | | | | (<i>trans</i>) | 50 | 609 |
| C ₁₄ H ₂₅ N ₂ O ₄ | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₄ CHMe- | | ... | 67 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₂ CHMe(CH ₂) ₂ - | | ... | 89 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₃ CHMeCH ₂ - | | ... | 61 | 434 |
| C ₁₄ H ₂₅ N ₂ O ₅ | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₂ CH(OMe)(CH ₂) ₂ - | | ... | 42 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₄ CH(OMe)- | | ... | 40 | 434 |
| C ₁₄ H ₂₆ N ₃ O ₃ | Me ₂ N(CH ₂) ₂ NHCO | H | H | -(CH ₂) ₃ CHMeCH ₂ - | | ... | 34 | 434 |
| C ₁₅ H ₂₇ N ₂ O ₄ | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₇ - | | ... | 70 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -CH ₂ CHMeCH ₂ CHMeCH ₂ - | | ... | 82 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -CH ₂ CHMeCHMe(CH ₂) ₂ - | | ... | 75 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₂ CHEt(CH ₂) ₂ - | | ... | 75 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₂ CMe ₂ (CH ₂) ₂ - | | ... | 73 | 434 |
| C ₁₆ H ₂₉ N ₂ O ₄ | Et ₂ N(CH ₂) ₂ OCO | H | H | -(CH ₂) ₃ CHMeCH ₂ - | | ... | 56 | 434 |
| C ₁₇ H ₁₇ NO ₃ | Me | H | H | <i>m</i> -PhCH ₂ OC ₆ H ₄ | H | 65-66 (EtOH) | 50 | 527 |
| | Me | H | H | <i>p</i> -PhCH ₂ OC ₆ H ₄ | H | 101-102 | .. | 527 |
| C ₁₇ H ₁₇ NO ₄ | <i>p</i> -MeOC ₆ H ₄ CH ₂ | Me | H | Ph | H | <i>cis</i> | 70 | 609 |
| | | | | | | <i>trans</i> | 75 | 609 |
| | PhOCH ₂ CH ₂ | Me | H | Ph | H | <i>cis</i> , 55-57 | 51 | 609 |
| | | | | | | <i>trans</i> , 113-115 | 54 | 609 |
| C ₁₈ H ₃₀ N ₂ O ₄ | Me ₂ N(CH ₂) ₂ OCO | H | H | <i>trans</i> -2-Decahydro-naphthyl | H | ... | 60 | 434 |
| | Me ₂ N(CH ₂) ₂ OCO | H | H | <i>cis</i> -2-Decahydro-naphthyl | H | ... | 77 | 434 |
| C ₂₁ H ₁₉ NO ₂ | α -Naphthylmethylene | Me | H | Ph | H | <i>cis</i> , 117-118 | 55 | 609 |
| | | | | | | <i>trans</i> , 120-125 | 57 | 609 |

Structure



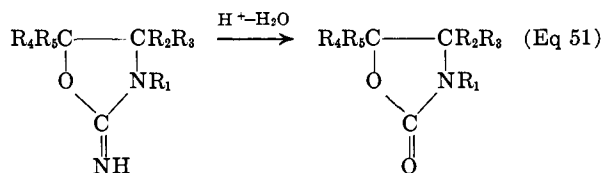
125-126

.. 334



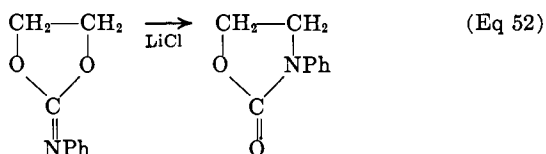
182-183

.. 334



S. FROM 2-IMINO-1,3-DIOXOLANE

The literature cites one case (217) of a 2-phenylimino-1,3-dioxolane rearranging to form a 2-oxazolidone when treated with lithium chloride (Eq 52)



T. MISCELLANEOUS (TABLE XXXIX)

There are a number of preparations of 2-oxazolidones given in the literature in which the method of cyclization or the starting material, or both, is unclear. These miscellaneous preparations are placed together in Table XXXIX, although some of the compounds may be listed in earlier tables if their preparation has been clearly described.

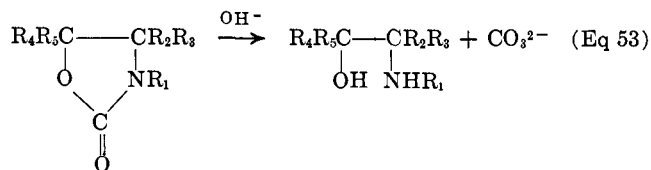
III. REACTIONS OF 2-OXAZOLIDONES

A. DECOMPOSITION AND RING-OPENING REACTIONS

1. Reactions with Bases

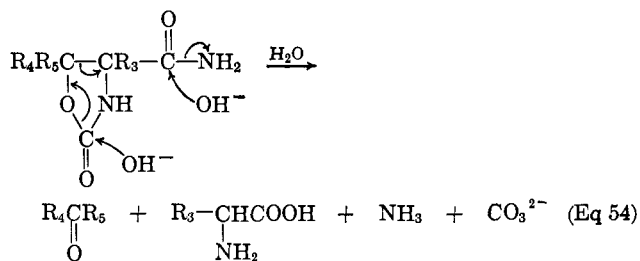
a. With Hydroxylic Bases

Hydrolysis with sodium hydroxide or potassium hydroxide yields a β -amino alcohol (Eq 53). These



hydrolyses are commonly carried out in aqueous (5, 21, 212, 332, 610) or alcoholic (5, 479, 589) systems, although potassium hydroxide in dioxane has also been used (211). Generally, alkaline hydrolyses have been used to prove structure or to establish stereochemistry (5, 21, 107, 209–212, 221, 235, 325, 479, 609).

An interesting decomposition occurs when an amide-substituted 2-oxazolidone is attacked by aqueous base (Eq 54) (235).

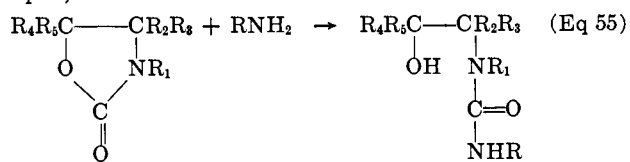


b. With Lithium Aluminum Hydride

Reduction of 2-oxazolidones with lithium aluminum hydride yields the corresponding β -amino alcohols (321, 325, 376, 608). The reaction is stereospecific (608).

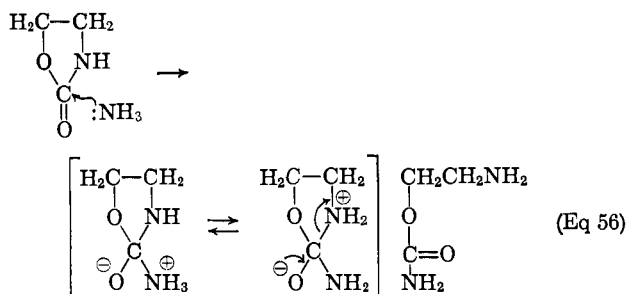
c. With Nitrogenous Bases and Ammonia

When 2-oxazolidones are attacked by equimolar amounts of primary aliphatic amines, the major product is an N,N' -disubstituted urea (370, 371) (Eq 55)



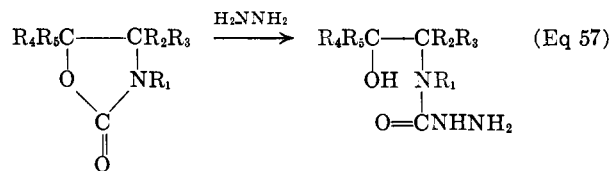
When aromatic primary amines or aliphatic amines are used, such as benzylamine, the products of ring opening are an N,N' -disubstituted urea and a 2-imidazolidone.

When 2-oxazolidone itself is treated with aqueous ammonia, β -aminoethyl carbamate is the product (Eq 56) (536).



d. With Hydrazine

Reaction with hydrazine yields a semicarbazide (607). The reaction proceeds in 90% yield in the case of *cis*-4-methyl-5-phenyl-2-oxazolidone and is reported to be stereospecific (Eq 57).



e. Alkaline Decomposition of N-Nitroso-2-oxazolidones

The pioneering work was done by Gabriel (190) who observed that *N*-nitroso-2-oxazolidone on heating with strong base gave acetylene, carbon dioxide, nitrogen, and water. Later investigators found that *N*-nitrosooxazolidones substituted in the 5-position yielded a mixture of products including acetylenes, ketones, aldehydes, and vinyl ethers (156, 381, 383, 384).

When the *N*-nitroso-2-oxazolidone was substituted at the 4-position, reaction with hydroxide ion yielded aldehydes, alcohols, and carbonates (156, 382).

With *p*-anisidine or *p*-phenetidine, the products of decomposition of *N*-nitroso-2-oxazolidone were 2-*p*-anisyl- (or phenetidyl-) aminoethyl *N*-*p*-anisyl- (or phenetidyl-) carbamate and *N,N'*-di-*p*-anisyl- (or phenetidyl-) ethylenediamine, plus carbon dioxide, nitrogen, and traces of acetaldehyde and acetylene (342).

With benzylamine in ethanol, *N*-nitroso-2-oxazolidone yielded ethylene glycol bis-*N*-benzylcarbamate, 2-benzylaminoethyl *N*-benzylcarbamate, 2-hydroxyethyl *N*-benzylcarbamate, and *N,N'*-dibenzylethylenediamine, together with traces of benzyl alcohol (99).

2. Reactions with Acids

When concentrated or dilute aqueous hydrochloric acid is used to decompose 2-oxazolidones, the products are hydrochlorides of β -amino alcohols (28, 41, 55, 224, 257, 283, 357, 419, 527, 598); with anhydrous gaseous hydrogen chloride, the product is the hydrochloride of a β -chloramine (56, 515, 559).

3. Pyrolytic Decomposition

a. N-Nitroso-2-oxazolidones

Pyrolysis of *N*-nitroso-substituted oxazolidones has given evidence of evolution of carbon dioxide, carbon monoxide, and nitrogen. The chief nongaseous products are the parent oxazolidone, as well as aldehydes and ketones in smaller amounts (156, 382, 591). Other studies suggest that acetylenes and ethylenes are also formed (385).

b. Other 2-Oxazolidones

When 2-oxazolidone itself is heated, carbon dioxide is evolved and polyethylenimine is formed (110, 278, 486, 516). If, however, an amine, such as triethanolamine (516), or a polyamide (486) is present, polymerization is prevented and a smooth decomposition into ethylenimine and carbon dioxide ensues.

N-Dodecyl-2-oxazolidone heated *in vacuo* evolves carbon dioxide and affords a polymer (531). N-Amino-2-oxazolidone heated to 175° forms polyethylenehydrazine and evolves carbon dioxide (167). Other N-substituted 2-oxazolidones are believed to produce low molecular weight polymers of the corresponding ethylenimine upon pyrolysis (396).

Only one study of the kinetics of pyrolytic decarboxylation of 2-oxazolidones is reported (397). Apparently the fission of the nitrogen-carbon bond of the urethan group is the rate-determining step.

4. Miscellaneous Decompositions

4-Methyl-4-hydroxymethyl-2-oxazolidone on treatment with phosgene in dioxane is reported to yield the carbamate (417).

B. SUBSTITUTION ON THE RING

1. Alkylation at Nitrogen (Table XL)

Alkylation at the ring nitrogen has been effected in various ways, but usually under basic conditions, thus attesting to the acidity of the hydrogen atom attached to the endocyclic nitrogen. Alkylations have been carried out in the presence of potassium carbonate (532), sodium hydroxide, sodium methoxide, sodium hydride, sodium metal (12, 97, 419, 535, 610), and potassium (38). The alkylating agents have been chlorides (97, 468, 532, 610), bromides (12, 535), iodides (419, 478), sulfates (55, 209, 472), and even olefins (38, 326).

Another group of alkylations at nitrogen utilizes ethers as the alkylating agents, together with such catalysts as benzoic acid with mercuric acetate (576), benzyl alcohol with mercuric acetate (586a), mercuric acetate alone (586), sulfuric acid (413), and hydrochloric and sulfuric acids (241).

2. Acylation and Carbamylation at Nitrogen (Table XLI)

The endocyclic nitrogen has been acylated in both acidic (309) and basic (250) media. Carbamylation has been effected by reaction with phosgene in basic medium, followed by reaction with ammonia (97).

3. Nitrosation, Nitration, and Amination at Nitrogen (Table XLII)

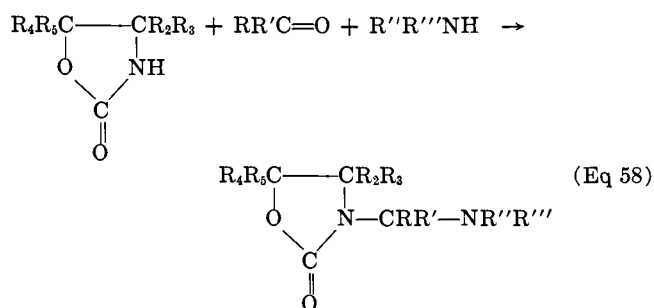
Nitrosation has been carried out with nitrous acid (156, 381, 382, 425) and nitrosyl chloride (156, 382).

Nitration has been accomplished with nitric acid in both sulfuric acid (60, 90) and acetic anhydride (90). The nitro group has been reduced to the amine electrolytically (195), by hydrogenation in the presence of platinum oxide in acid medium (195, 205), and by reaction with zinc and hydrochloric acid (425).

4. Reaction with Carbonyl Compounds (Table XLIII)

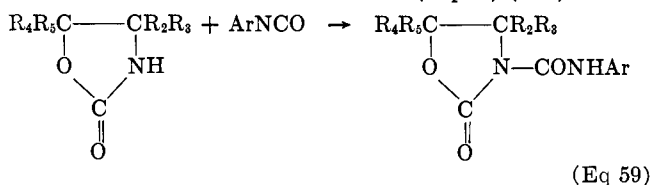
2-Oxazolidones react with carbonyl compounds in the presence of added amine in a manner analogous to the Mannich reaction (34) (Eq 58). In the absence of added amine, a second molecule of oxazolidone serves

as the amine (Eq 58, $R''R'''NH = \overline{OCOCH_2CH_2N-}$). In one recorded instance a hydroxy compound is produced (57).



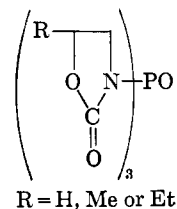
5. Reaction with Aryl Isocyanates (Table XLIV)

Reaction of substituted 2-oxazolidones with aryl isocyanates in the presence of pyridine or triethylamine yields 2-oxazolidone-3-carbanilides (Eq 59) (487).



6. Reaction with Phosphorus Compounds


The sodio derivative of substituted 2-oxazolidones reacts with phosphorus oxychloride in dimethylformamide under nitrogen to give substituted phosphorus compounds of the following type (112)



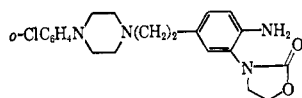
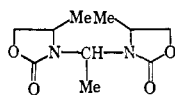
C. REACTIONS OF GROUPS ON THE RING

Although many reactions do not involve the 2-oxazolidone ring itself, they are included here for the sake of completeness.

TABLE XL
 N-ALKYLATED 2-OXAZOLIDONES

| Empirical formula ^a | R ₁ | R ₂ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|------------------------------------|----------------|---|--|--|---------|-----------------------|
| C ₅ H ₇ NO ₂ | CH ₂ =CH | H | H | H | 76.5-78.0 (0.5), 90-96 (1-2) | 28 | 586, 586a |
| C ₅ H ₉ NO ₃ | HOCH ₂ CH ₂ | H | H | H | ... | .. | 332 |
| C ₆ H ₈ N ₂ O ₂ | NCCH=CH | H | H | H | ... | .. | 468 |
| C ₆ H ₇ NO ₂ | HC≡CCH ₂ | H | H | H | 68-69 (0.39-0.40) | .. | 535 |
| C ₆ H ₈ N ₂ O ₂ | NCCH ₂ CH ₂ | H | H | H | Oil | 93 | 326 |
| C ₆ H ₉ NO ₂ | CH ₂ =CH | H | Me | H | 78-81 (1.3) 105-108 (2.5) | 86 | 38, 413, 586, 586a |
| C ₈ H ₁₁ NO ₂ | Me | H | Me | Me | 128-132 (24) | 51 | 97 |
| C ₇ H ₉ NO ₂ | HC≡CCH ₂ | H | Me | H | 35-36 (EtOH-H ₂ O) | .. | 535 |
| C ₇ H ₁₁ NO ₂ | CH ₂ =CHCH ₂ | H | Me | H | 80 (0.4) | .. | 539 |
| | CH ₂ =CH | H | Et | H | 82-90 (0.7) | 45 | 586 |
| C ₈ H ₁₃ NO ₂ | CH ₂ =CHCH ₂ | H | Et | H | ... | .. | 539 |
| | CH ₂ =CHCH ₂ | H | Me | Me | ... | .. | 539 |
| C ₈ H ₁₅ NO ₂ | Me | H | Et | Et | 92-94 (0.3) | 68 | 97 |
| C ₉ H ₁₈ N ₂ O ₂ | Me | H | Et ₂ NCH ₂ | H | HI salt, 160.5-161.5 | 68 | 478 |
| C ₁₀ H ₁₁ NO ₂ | PhCH ₂ | H | H | H | 78 | .. | 532 |
| | Me | H | Ph | H | ... | .. | 97 |
| C ₁₀ H ₁₅ NO ₂ | Me | H |  | H | 110-115 (0.029) | 72 | 209 |
| C ₁₀ H ₁₉ NO ₂ | Isoamyl | H | Me | Me | 102-104 (0.3) | 75 | 97 |
| C ₁₁ H ₁₁ NO ₂ | CH ₂ =CH | H | Ph | H | 79.5-80.5 | 25 | 586 |
| C ₁₁ H ₁₂ NO ₃ Cl | Me | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | H | 79-81 | .. | 12 |
| | Me | H | <i>m</i> -ClC ₆ H ₄ OCH ₂ | H | ... | .. | 12 |
| C ₁₁ H ₁₃ NO ₃ | Me | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | 75 (Et ₂ O) | 78 | 55 |
| | Me | H | <i>m</i> -MeOC ₆ H ₄ OCH ₂ | H | ... | .. | 55 |
| C ₁₂ H ₁₃ NO ₂ | CH ₂ =CHCH ₂ | H | Me | Me | ... | .. | 539 |
| C ₁₂ H ₁₅ NO ₂ | Et | Me | Ph | H | ... | 44 | 589 |
| | Me | H | Ph | Et | 141-142 (0.25) | 78 | 97 |
| C ₁₂ H ₁₅ NO ₃ | Me | H | <i>m</i> -MeC ₆ H ₄ OCH ₂ | H | 73.5 | .. | 12 |
| C ₁₂ H ₁₆ NO ₄ | Me | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 72.5-75 (C ₆ H ₆ -Et ₂ O) | .. | 12 |
| | Me | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | ... | .. | 12 |
| C ₁₂ H ₁₅ NO ₅ | Me | H | 3,4-(MeO) ₂ C ₆ H ₃ | H | ... | .. | 419 |
| C ₁₃ H ₁₇ NO ₄ | Et | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 175-178 (0.1) | .. | 12 |
| C ₁₆ H ₂₁ N ₂ O ₂ | β -N-Pyrrolidino-ethyl | Me | Ph | H | <i>trans</i> , 126-128 | .. | 610 |
| C ₁₆ H ₂₂ N ₂ O ₃ | β -N-Morpho- linoethyl | Me | Ph | H | <i>cis</i> , 86-89; <i>trans</i> , 60-62 | .. | 610 |
| C ₁₇ H ₁₇ NO ₃ | Me | H | <i>p</i> -PhCH ₂ OC ₆ H ₄ | H | 101-102 (EtOH) | 76 | 55 |
| | Me | H | <i>m</i> -PhCH ₂ OC ₆ H ₄ | H | 65-66 (dil EtOH) | 80 | 55 |
| C ₁₇ H ₂₃ N ₂ O ₂ | β -N-Piperidino-ethyl | Me | Ph | H | <i>cis</i> , 95-96; <i>trans</i> , 49-52 | .. | 610 |
| C ₂₀ H ₂₄ NO ₆ | Me | H | 3,4-(MeO) ₂ C ₆ H ₃ | 3,4-(MeO) ₂ C ₆ H ₃ | 118-120 (Et ₂ O-MeOH) | 96 | 472 |

Structure

168-169 (*i*-PrOH) .. 30

223.5 .. 74 241

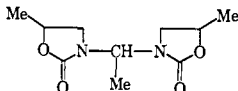
198-199 (Me₂CO) 7 576^a R₃ = H.

TABLE XLI

N-ACYLATED AND CARBAMYLATED 2-OXAZOLIDONES

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Mp, °C | % yield | Ref |
|---|--------------------------------------|----------------|----------------|----------------|----------------|--|---------|-----|
| C ₅ H ₇ NO ₃ | MeCO | H | H | H | H | 69-70 (Skellysolve B-Et ₂ O) | .. | 250 |
| C ₆ H ₉ NO ₂ | CH ₂ =CH | H | H | Me | H | ... | 14 | 309 |
| C ₆ H ₁₀ N ₂ O ₃ | H ₂ NCO | H | H | Me | Me | 118-120 (EtOH) | 48 | 97 |
| C ₇ H ₁₁ NO ₃ | MeCO | H | H | Me | Me | 42.5-44 (EtOH-Skellysolve B) | 75 | 97 |
| C ₈ H ₁₃ NO ₄ | EtOCO | H | H | Me | Me | 54-55.5 (Et ₂ O-Skellysolve B) | 79 | 97 |
| C ₈ H ₁₄ N ₂ O ₃ | H ₂ NCO | H | H | Et | Et | 82-84 (C ₆ H ₆ -Skellysolve B) | 78 | 97 |
| C ₉ H ₁₄ NO ₃ | Me ₂ CCO | H | H | Me | Me | 80-81 (Skellysolve B) | 48 | 97 |
| C ₉ H ₁₆ N ₂ O ₃ | H ₂ NCO | Me | Me | Pr | H | 102-105 (EtOH) | 55 | 97 |
| C ₁₀ H ₁₀ N ₂ O ₃ | H ₂ NCO | H | H | Ph | H | 132.5-133.5 (EtOH) | 67 | 97 |
| C ₁₀ H ₁₇ NO ₃ | MeCO | Me | Me | Pr | H | 29.5-30 (Skellysolve B) | 80 | 97 |
| | Me ₂ CHCH ₂ CO | H | H | Me | Me | 49.5-51 (Skellysolve B) | 70 | 97 |
| C ₁₁ H ₁₂ N ₂ O ₃ | H ₂ NCO | H | H | Ph | Me | 113-114 (EtOH) | 54 | 97 |
| C ₁₂ H ₁₄ N ₂ O ₃ | H ₂ NCO | H | H | Ph | Et | 112-113 (C ₆ H ₆ -Skellysolve B) | 63 | 97 |
| C ₁₆ H ₁₄ N ₂ O ₃ | H ₂ NCO | H | H | Ph | Ph | 181-185 (EtOH) | 68 | 97 |
| C ₁₇ H ₁₆ NO ₃ | MeCO | H | H | Ph | Ph | 142-143 (EtOH) | 76 | 97 |

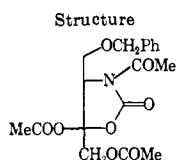
99-100 (THF-*i*-Pr₂O) 88 211

TABLE XLII

N-NITROSO-, N-NITRO-, AND N-AMINO-2-OXAZOLIDONES

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|---|------------------|------------------------------------|----------------------------------|------------------------------------|----------------|------------------------------|---------|----------|
| C ₃ H ₄ N ₂ O ₃ | ON | H | H | H | H | 100 | .. | 383, 425 |
| C ₃ H ₄ N ₂ O ₄ | O ₂ N | H | H | H | H | ... | .. | 195 |
| C ₃ H ₆ N ₂ O ₂ | H ₂ N | H | H | H | H | 69-71 (EtOH) | 55 | 195, 425 |
| C ₅ H ₆ N ₄ O ₁₀ | O ₂ N | O ₂ NOCH ₂ | O ₂ NOCH ₂ | H | H | 122-123 | 30 | 60 |
| C ₅ H ₈ N ₂ O ₃ | ON | H | H | Me | Me | 87.9-89.8 | 71 | 383 |
| | ON | Me | Me | H | H | 95.8-96.4 | 70 | 156, 382 |
| | ON | Et | H | H | H | 110 (1) | 84 | 156, 382 |
| C ₅ H ₈ N ₂ O ₄ | O ₂ N | Me | Me | H | H | ... | .. | 201 |
| C ₅ H ₁₀ N ₂ O ₂ | H ₂ N | Me | Me | H | H | 130-135 (10) | .. | 201 |
| C ₇ H ₁₂ N ₂ O ₂ | ON | H | H | Et | Et | ... | .. | 383 |
| C ₈ H ₁₂ N ₂ O ₃ | ON | H | H | -(CH ₂) ₆ - | H | 82.5-83.2 | 94 | 381, 383 |
| | ON | -(CH ₂) ₅ - | H | H | H | 107.5-108.5 | 99 | 156, 382 |
| C ₈ H ₈ N ₂ O ₂ | ON | Ph | H | H | H | 83.8-84.6 | 80 | 156, 382 |
| | ON | H | H | Ph | H | 76.5-77.5 | 77 | 383 |
| C ₉ H ₁₂ N ₂ O ₃ | O ₂ N | MeCOOCH ₂ | MeCOOCH ₂ | H | H | 97.1-97.8 | .. | 90 |
| C ₉ H ₁₄ N ₂ O ₃ | ON | H | H | -(CH ₂) ₆ - | H | 82.6-83.5 | 93 | 383 |
| C ₁₀ H ₁₀ N ₂ O ₃ | ON | H | H | Ph | Me | 116.5-117.4 | 97 | 383 |
| | ON | Ph | Me | H | H | 84.6-86.0 | 98 | 156, 382 |
| C ₁₁ H ₁₂ N ₂ O ₃ | ON | H | H | Ph | Et | ... | .. | 383 |
| C ₁₅ H ₁₃ N ₂ O ₃ | ON | H | H | Ph | Ph | 107.5-108.5 | 92 | 383 |
| | ON | Ph | H | Ph | H | <i>erythro</i> , 115.2-117.5 | 89 | 383 |
| | | | | | | <i>threo</i> , 106.5-108.0 | 91 | 383 |
| | ON | Ph | Ph | H | H | 100.2-101.0 | 91 | 156, 382 |
| C ₂₃ H ₁₇ N ₂ O ₂ | ON | Ph | Ph | Ph | H | 115.8-117.5 | 91 | 383 |

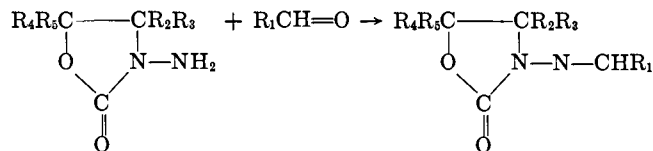
1. Reaction of *N*-Amino Groups

a. Reaction with Carbonyl Compounds and Carbonyl Precursors (Table XLV)

Heating *N*-amino-2-oxazolidones with carbonyl compounds in a solvent produces Schiff bases (275, 301, 418, 522, 524) (Eq 60). In only one case was a catalyst used (ZnCl₂) (418).

Besides the free carbonyl compounds, the diacetate (234, 307, 402) and the oxime (204) have been used.

Reactions have also been conducted on benzylidene-amino (142), methyleneamino (234, 402), and acetyl-amino derivatives (234) of the oxazolidone.



(Eq 60)

TABLE XLIII
 REACTION PRODUCTS OF 2-OXAZOLIDONES WITH CARBONYL COMPOUNDS

| Empirical formula ^a | Substitution at 3-position | Bp (mm) or mp, °C | % yield | Ref |
|--|--|-----------------------------|---------|-----|
| C ₅ H ₆ N ₂ O ₃ Cl ₃ ^b | Cl ₃ CCH(OH) | 134-136 (CCl ₄) | .. | 57 |
| C ₈ H ₁₂ N ₂ O ₂ | Me ₂ NCH ₂ | 90 (0.2) | 84 | 34 |
| C ₈ H ₁₄ N ₂ O ₂ | N-Pyrrolidinomethyl | 123 (0.2) | .. | 34 |
| C ₈ H ₁₆ N ₂ O ₂ | Et ₂ NCH ₂ | 107 (0.2) | 80 | 34 |
| C ₁₂ H ₂₄ N ₂ O ₂ | Bu ₂ NCH ₂ | 130-132 (0.4) | 80 | 34 |
| C ₁₃ H ₁₉ N ₂ O ₂ | PhCH ₂ N(Me) ₂ CH ₂ | 152 | .. | 34 |

| Empirical formula ^c | R | R ₄ | MP, °C | % yield | Ref |
|---|----|---------------------|----------------------------|---------|-----|
| C ₇ H ₁₀ N ₂ O ₄ | H | H | 99-100 (EtOAc) | 91 | 258 |
| C ₈ H ₁₂ N ₂ O ₄ | Me | H | .. | .. | 258 |
| C ₉ H ₈ N ₂ O ₄ Cl ₅ | H | Cl ₃ C | 129-134 (H ₂ O) | 55 | 258 |
| C ₉ H ₁₀ N ₂ O ₆ | H | OCH | 197 dec | .. | 258 |
| C ₉ H ₁₄ N ₂ O ₄ | H | Me | 152-155 | 93 | 258 |
| C ₁₀ H ₁₆ N ₂ O ₄ | Me | Me | 195.5-198.5 (MeOH) | .. | 258 |
| C ₁₁ H ₁₆ N ₂ O ₄ | H | CH ₂ =CH | Oil | .. | 258 |
| C ₁₁ H ₁₈ N ₂ O ₄ | H | Et | 123-126 | .. | 258 |
| C ₁₃ H ₁₈ N ₂ O ₄ | H | MeCH=CH | Oil | .. | 258 |
| C ₁₅ H ₁₆ N ₂ O ₆ | H | 2-furyl | 138-141 | .. | 258 |
| C ₁₆ H ₂₆ N ₂ O ₄ | H | <i>n</i> -Bu | 96-98 | .. | 258 |
| C ₁₉ H ₁₈ N ₂ O ₄ | H | Ph | 125-127 (MeOH) | .. | 258 |
| C ₂₃ H ₂₂ N ₂ O ₄ | H | PhCH=CH | 128 | .. | 258 |

^a R₂ = R₃ = R₄ = R₅ = H. ^b No added amine. ^c R₂ = R₃ = R₅ = H.

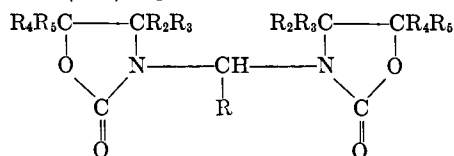
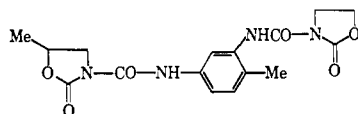


TABLE XLIV

2-OXAZOLIDONE-3-CARBANILIDES FROM 2-OXAZOLIDONES AND ARYL ISOCYANATES (487)

| Empirical formula ^a | R ₄ | R ₅ | Ar | MP, °C | % yield |
|--|----------------|----------------|--|---------|---------|
| C ₁₀ H ₁₀ N ₂ O ₃ | H | H | Ph | 114-115 | 82 |
| C ₁₁ H ₁₁ N ₂ O ₃ Cl | H | Me | <i>p</i> -ClC ₆ H ₄ | 130-132 | 40 |
| C ₁₁ H ₁₂ N ₂ O ₃ | H | Me | Ph | 139-140 | 76 |
| C ₁₁ H ₁₂ N ₂ O ₄ | H | H | <i>p</i> -MeOC ₆ H ₄ | 143-144 | 50 |
| C ₁₂ H ₁₄ N ₂ O ₃ | Me | Me | Ph | 152-153 | 69 |
| | H | Et | Ph | 113-114 | 57 |
| C ₁₂ H ₁₄ N ₂ O ₄ | H | Me | <i>p</i> -MeOC ₆ H ₄ | 138-139 | 37 |

Structure

^a R₂ = R₃ = H.

b. Other Reactions (Table XLVI)

Reaction of the N-amino group with potassium thiocyanate gives substituted thioureas (150, 151). With acetic anhydride acetamides are obtained (233), and with acid chlorides other amides result (453).

 2. Elimination Reactions to
 Produce N-Vinyl Groups

N-β-Chloroethyl-2-oxazolidone has been dehydrohalogenated with sodium oxide in benzene (23) or with potassium *t*-butoxide (218) to give N-vinyl-2-oxazolidone: mp 15°, bp 70° (0.1 mm), 100-105° (1.3 mm). Pyrolysis of N-(β-acetoxyethyl)-2-oxazolidone (299)

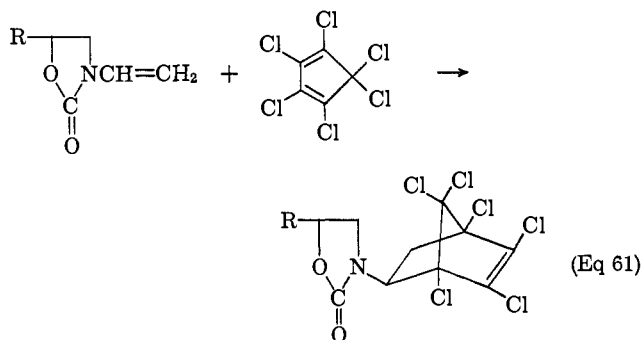
eliminates acetic acid, also giving the N-vinyl derivative in 71% yield.

Heating di(2-oxazolidon-3-yl)methylmethane under reduced pressure alone or in the presence of catalysts, such as aluminum chloride or zinc chloride, gives vinyl-2-oxazolidone in 42% yield (259). The same decomposition has been effected with zinc oxide or with γ-collidine (573) on the 5-methyl-2-oxazolidone derivative to give the corresponding N-vinyl compounds.

3. Reactions of N-Vinyl Groups

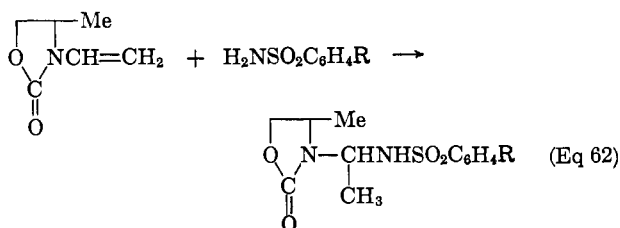
N-Vinyl-2-oxazolidones undergo addition and polymerization reactions. Thus Diels-Alder reaction with

hexachlorocyclopentadiene yields the adducts shown in Eq 61 (438).



R = H, mp 172–174°
 R = Me, mp 219–221°
 R = Et, mp 153.0–153.5°

Benzenesulfonamide and *p*-toluenesulfonamide have been added to the N-vinyl group (Eq 62) (242).



R = H, mp 145–148 (93% yield)
 R = *p*-Me, mp 151–153° (91% yield)

Poly(N-vinyl-2-oxazolidone) is formed in 98% yield by polymerization of the monomer with azobis(isobutyronitrile) as initiator (299).

N-Vinyl-2-oxazolidone reacts with 2-oxazolidone to yield N,N'-ethylidenebis(2-oxazolidone) (299). The N-vinyl derivative is sensitive to aqueous acids, yielding 2-oxazolidone readily (299).

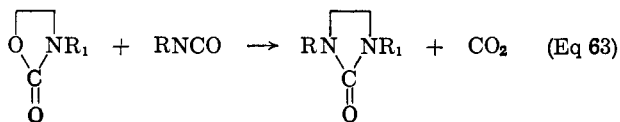
4. Miscellaneous Reaction Products

A miscellaneous group of reaction products is listed in Table XLVII.

D. OTHER REACTIONS OF THE RING

In an early paper (191), it is reported that 2-oxazolidone reacts with aniline to form water, 3-phenyl-2-oxazolidone, mp 124°, and 1-phenyl-2-imidazolidone, mp 157–158°. More recent papers (193, 340) describe the synthesis of 1-benzyl-2-imidazolidone in 17% yield from 2-oxazolidone and benzylamine.

Reaction of N-substituted 2-oxazolidones with organic isocyanates yields N,N'-disubstituted 2-imidazolidones (Eq 63) (31). The reaction is catalyzed by lithium chloride and is accompanied by evolution of carbon dioxide.



E. FORMATION OF MOLECULAR COMPLEXES

2-Oxazolidones form molecular complexes with the halogens (84, 193, 213, 541, 572), with IBr (541), with sulfur trioxide (480), and with 5-nitro-2-furaldehyde (202). The sulfur trioxide complex (480) can be used as a sulfonation reagent for compounds sensitive to oxidation. The complex with 5-nitro-2-furaldehyde has a characteristic ultraviolet absorption at 310 m μ .

IV. PHYSICAL CHEMISTRY AND PROPERTIES

A. PROPERTIES

In general, 2-oxazolidones are stable solids (104, 109). The parent compound is water soluble and forms an essentially neutral solution.

The five-membered ring is not readily reduced by sodium in alcohol. It can be nitrated with nitric acid-sulfuric acid mixtures, and it is not attacked by phosphorus trichloride (109). Its basicity is so slight that neither hydrochlorides nor picrates can be isolated. It does not react with bromine (250).

B. SPECTRAL CHARACTERISTICS

1. Infrared

A number of studies have been published on the infrared characteristics of 2-oxazolidones (223, 344, 345, 421, 422). A larger number of papers have reported characteristic infrared bands of the 2-oxazolidone ring incidental to other work (50, 111, 240, 256, 275, 304, 386, 441, 442, 471, 477, 592). The carbonyl absorption is generally of fairly high energy, usually falling in the range 1740–1810 cm⁻¹ and very often at wavenumbers above 1760 cm⁻¹. In addition it is reported that the 2-oxazolidone ring has a characteristic absorption band at 1029–1059 cm⁻¹ (421, 422). Unpublished work in this laboratory has shown that 2-oxazolidone and other 2-oxazolidones with no substituent group on nitrogen show a weak doublet in the 3200–3500-cm⁻¹ region, suggesting that they may exist as a mixture of keto and enol forms.

2. Ultraviolet

Most activity has centered about the pharmaceutically important nitrofurans and compounds related to them chemically (153, 159–161, 202, 327). Ultraviolet data have been reported for a 2-oxazolidone moiety attached to a steroidal nucleus (353).

3. Nuclear Magnetic Resonance

There is a paucity of nuclear magnetic resonance data, though a few fairly detailed analyses have been made (255, 353, 482, 504). One study used nmr to establish the configuration of the diastereomeric 2-oxazolidone derivatives of the ephedrine (255).

TABLE XLV
 SCHIFF BASES FROM N-AMINO-2-OXAZOLIDONES AND CARBONYL COMPOUNDS

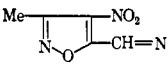
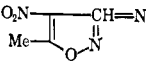
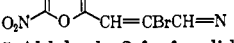
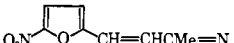
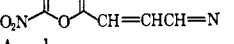
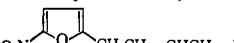
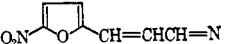


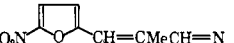

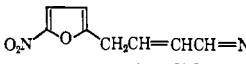
| Empirical formula ^a | R ₁ | R ₄ | Mp °C | % yield | Ref |
|--|---|--|--|---------|---|
| C ₄ H ₆ N ₂ O ₂ | CH ₂ =N | H | 96 (MeOH) | .. | 233, 402 |
| C ₈ H ₇ N ₂ O ₃ Br | 5-Bromo-2-furfurylideneamino | H | 179-182 (MeOH) | 88 | 524 |
| C ₈ H ₇ N ₂ O ₃ I | 5-Iodo-2-furfurylideneamino | H | 191-193 (MeOH) | 90 | 524 |
| C ₈ H ₇ N ₂ O ₅ | 5-Nitro-2-furfurylideneamino | H | 230, 246-248, 254-256 (<i>i</i> -PrOH) | 96 | 71, 93, 142, 204, 234, 307, 402, 424, 425, 443, 558 |
| C ₈ H ₈ N ₂ O ₅ |  | H | 188-189 (aq EtOH) | .. | 85 |
| |  | H | 220-222 dec (EtOH) | .. | 85 |
| C ₉ H ₉ N ₂ O ₂ Cl | 5-Chloromethyl-2-furfurylideneamino | H | 159-162 | 90 | 275 |
| C ₉ H ₁₀ N ₂ O ₃ | 5-Methyl-2-furfurylideneamino | H | 138-140 (50% MeOH) | 71 | 524 |
| C ₁₀ H ₉ N ₂ O ₅ | 5(β-Nitrovinyl)-2-furfurylideneamino | H | 227-229 (MeNO ₂) | 58 | 275 |
| C ₁₀ H ₉ N ₂ O ₅ Br |  | H | 246-248 dec | .. | 301 |
| C ₁₀ H ₁₀ N ₂ O ₄ | 5-Aldehyde-2-furfurylideneamino | H | 195-200 (MeNO ₂) | 61 | 275 |
| C ₁₁ H ₁₁ N ₂ O ₅ |  | H | 164-166.5 (EtOH) | 96 | 418 |
| | 5(β-Nitro-β-methylvinyl)furfurylideneamino | H | 212-214 (MeNO ₂) | 20 | 275 |
| C ₁₁ H ₁₄ N ₂ O ₄ | 5-Ethoxymethyl-2-furfurylideneamino | H | 121 (EtOH) | .. | 275 |
| C ₁₃ H ₁₆ N ₂ O ₄ Br | 5-Bromo-2-furfurylideneamino | N-Morpholinomethyl | 200-202 (MeOH) | 84 | 522 |
| C ₁₃ H ₁₆ N ₂ O ₄ I | 5-Iodo-2-furfurylideneamino | N-Morpholinomethyl | 209-210 (Me ₂ CO) | 80 | 522 |
| C ₁₃ H ₁₆ N ₂ O ₆ | 5-Nitro-2-furfurylideneamino | N-Morpholinomethyl | 204-206 (EtOH), 206-208 | .. | 208, 522 |
| C ₁₃ H ₁₇ N ₂ O ₄ | 2-Furfurylideneamino | N-Morpholinomethyl | 164-165 (MeOH) | 84 | 522 |
| C ₁₃ H ₁₇ N ₄ O ₅ |  | Me ₂ NCH ₂ | 216-217 | .. | 199 |
| C ₁₄ H ₁₃ N ₄ O ₆ | As above | N-Morpholinomethyl | 230-232 | .. | 199 |
| C ₁₄ H ₁₉ N ₂ O ₄ | 5-Methyl-2-furfurylideneamino | N-Morpholinomethyl | 182-183 (MeOH) | 93 | 522 |
| C ₁₄ H ₁₉ N ₄ O ₅ |  | Me ₂ NCH ₂ | 120.5-121.5 | .. | 199 |
| C ₁₅ H ₁₄ N ₄ O ₅ |  | N-Pyrrolidinomethyl | 211-212 | .. | 199 |
| C ₁₅ H ₁₅ N ₄ O ₆ |  | N-Morpholinomethyl | 170-172 | .. | 199 |
| C ₁₅ H ₁₈ N ₃ O ₃ Cl | <i>o</i> -ClC ₆ H ₄ CH=N | N-Morpholinomethyl | 122-123 (50% MeOH) | 82 | 522 |
| | <i>p</i> -ClC ₆ H ₄ CH=N | N-Morpholinomethyl | 138-139 (50% MeOH) | 53 | 522 |
| C ₁₅ H ₁₈ N ₃ O ₃ Br | <i>o</i> -BrC ₆ H ₄ CH=N | N-Morpholinomethyl | 129-130 (50% MeOH) | 76 | 522 |
| | <i>p</i> -BrC ₆ H ₄ CH=N | N-Morpholinomethyl | 150-151 (50% MeOH) | 84 | 522 |
| C ₁₅ H ₁₈ N ₃ O ₃ I | <i>p</i> -IC ₆ H ₄ CH=N | N-Morpholinomethyl | 195-198 (Me ₂ CO) | 60 | 522 |
| C ₁₅ H ₁₈ N ₄ O ₅ | <i>p</i> -O ₂ NC ₆ H ₄ CH=N | N-Morpholinomethyl | 181-182 (MeOH) | 95 | 522 |
| | <i>m</i> -O ₂ NC ₆ H ₄ CH=N | N-Morpholinomethyl | 174-175 (MeOH) | 95 | 522 |
| | 5-Nitro-2-furfurylideneamino | N-Piperidinomethyl | 197-198 (EtOH) | .. | 203 |
| C ₁₅ H ₁₈ N ₃ O ₃ Br |  | N-Morpholinomethyl | 202-205 dec 195-196 (dioxane) | .. | 225, 301 |
| C ₁₅ H ₁₉ N ₂ O ₃ | PhCH=N | N-Morpholinomethyl | 168-169 (MeOH) | 68 | 522 |
| C ₁₅ H ₁₉ N ₂ O ₄ | <i>o</i> -HOC ₆ H ₄ CH=N | N-Morpholinomethyl | 191-192 (MeOH) | 68 | 522 |
| C ₁₆ H ₂₀ N ₃ O ₆ Br | 3-Br-4-MeOC ₆ H ₄ CH=N | N-Morpholinomethyl | 152-153 (50% Me ₂ CO) | 87 | 522 |
| C ₁₆ H ₂₀ N ₄ O ₆ |  | N-Morpholinomethyl | 176-176.5 (C ₆ H ₆ - <i>i</i> -PrOH) | .. | 225 |
| C ₁₆ H ₂₁ N ₃ O ₄ | <i>p</i> -MeOC ₆ H ₄ CH=N | N-Morpholinomethyl | 149-150 | 70 | 522 |
| C ₁₇ H ₁₆ N ₄ O ₆ Br |  | <i>o</i> -MeOC ₆ H ₄ O | 182-184 | .. | 301 |

TABLE XLV (Continued)

| Empirical formula ^a | R ₁ | R ₄ | Mp °C | % yield | Ref |
|---|---|----------------------------------|--------------------|---------|-----|
| C ₁₇ H ₂₂ N ₄ O ₅ |  5-Nitro-2-furfurylideneamino | N-Piperidinomethyl | 151-152 | .. | 199 |
| | | Bu ₂ NCH ₂ | 152.5-153.5 (EtOH) | .. | 203 |

^a R₂ = R₃ = R₅ = H.

TABLE XLVI

MISCELLANEOUS N-SUBSTITUTED 2-OXAZOLIDONES

| Empirical formula ^a | R ₁ | R ₄ | Mp, °C | % yield | Ref |
|---|---|----------------|----------------------------------|---------|-----|
| C ₅ H ₈ N ₂ O ₃ | MeCONH | H | 117 | .. | 233 |
| C ₁₆ H ₁₆ N ₃ O ₅ Cl ₃ | 3-H ₂ NSO ₂ -4-ClC ₆ H ₃ CONH | H | 182-183 (MeOH-Et ₂ O) | .. | 453 |
| C ₁₁ H ₁₂ N ₃ O ₅ Cl ₃ | 3-H ₂ NSO ₂ -4-ClC ₆ H ₃ CONH | Me | 215-216 (MeOH-Et ₂ O) | .. | 453 |

^a R₂ = R₃ = R₅ = H.

C. POLAROGRAPHY

Most, if not all, of the polarographic work has been on the N-(2-furfurylideneamino)-2-oxazolidone system because of its pharmaceutical importance. Much effort has been expended to discover methods for its determination in a large variety of media (29, 181, 327, 510-513, 563, 564).

D. DIPOLE MOMENTS

A few publications have appeared on the dipole moment of 2-oxazolidone and N-acetyl-2-oxazolidone (172, 173, 304). It has been concluded that a dipolar structure contributes about 21% to the experimentally found dipole moment (5.04 ± 0.05 D).

V. DETERMINATION OF 2-OXAZOLIDONES

Most work has been directed toward the determination of a few medicinally useful compounds in various media. An infrared method has been developed for determining 2-oxazolidone (111). A titrimetric method employing silver nitrate has been reported for determining 5-methyl-2-oxazolidone (111).

Among the methods used to determine 2-oxazolidone derivatives are: spectrophotometric (69, 245, 359, 507, 553, 612), colorimetric (46, 69, 157, 244, 372, 508), reaction with indole (372), chromatographic (69, 316), and methods based on the formation of a phenylhydrazone (79, 236). Oxazolidones have been analyzed in feeds (18, 19, 46, 79, 308, 315-317, 359, 509), urine (372), plasma (80), milk (106), chicken tissues (236), mixtures of pharmaceuticals (553, 612), and in the presence of impurities (245).

VI. STEREOCHEMISTRY

Several of the earlier studies centered about establishing the configuration of ephedrine (96, 176, 514, 590). The assignment of configuration depended on synthesis of 2-oxazolidones from a semicarbazide (514), a β-amino alcohol plus urea (96), a β-hydroxyhydrazide

plus nitrous acid (590), and an involved synthesis producing a 2-iminooxazolidone and its subsequent hydrolysis to a 2-oxazolidone (176).

A later scheme helped establish the configuration of monosaccharides. It utilized the stereospecific conversion of β-amino alcohols to 2-oxazolidones by reaction with diethyl carbonate (227). Japanese workers (261, 262) cyclized β-amino alcohols with urea and also with phosgene in order to assign configurations to the starting material. 2-Oxazolidones have been used to study the difference in rate of intramolecular migration in N-benzoylated derivatives of ephedrine and pseudo-ephedrine (589). Part of the proof of the absolute configuration of rotenone depended upon the formation of known derivatives of 2-oxazolidone (375). A study of the *threo* and *erythro* forms of threonine employed a synthesis of 2-oxazolidones from β-amino alcohols and phosgene together with acidic and basic hydrolyses (284).

French workers (358) obtained the hexahydrobenzo-2-oxazolidones containing both *cis* and *trans* ring fusions.

VII. APPLICATIONS

Many uses have been suggested for the 2-oxazolidones. These cannot be discussed in detail here and will only be summarized.

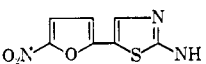
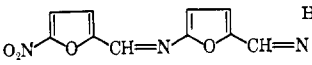
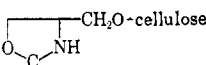
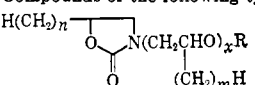
A. DRUGS AND OTHER BIOLOGICAL USES

1. Furazolidone

Considerable work has been done on Furazolidone or 3-(5-nitro-2-furfurylideneamino)-2-oxazolidone (alternate name, N-(5-nitro-2-furfurylidene)-3-amino-2-oxazolidone).

The effect of Furazolidone on poultry has been studied extensively (49, 87, 98, 103, 114, 130, 178, 185, 273, 338, 339, 427, 433, 440, 445, 483, 502, 606) with respect to growth, reproduction, and hatchability. Toxicity to poultry has been studied (136, 194) as

TABLE XLVII
 MISCELLANEOUS REACTION PRODUCTS

| Empirical formula | R ₁ | R ₂ | R ₃ | R ₄ | R ₅ | Bp (mm) or mp, °C | % yield | Ref |
|--|--|--|------------------------------------|---|----------------|--|---------|---------------|
| C ₇ H ₆ NO ₂ | H | H | H | H | H | 89-91 | 70 | 50, 462, 463 |
| C ₈ H ₄ N ₂ O ₂ | H ₂ N | H | H | H | H | ... | 80 | 443 |
| C ₄ H ₇ NO ₃ | H | H | H | MeO | H | ... | .. | 463 |
| C ₅ H ₈ NO ₂ Cl | H | ClCH ₂ | H | H | H | ... | .. | 13 |
| C ₇ H ₁₀ NO ₅ Cl ₂ P | (MeO) ₂ P(O)OC(=CCl ₂) | H | H | H | H | ... | .. | 466 |
| C ₇ H ₁₁ NO ₂ | Me | —CH ₂ — | Me | Me | Me | 58-62, 98 (1) | 75 | 132 |
| C ₇ H ₁₁ NO ₄ | MeCOO(CH ₂) ₂ | H | H | H | H | 52-54 (hexane-Et ₂ O) | 95 | 299 |
| C ₈ H ₇ N ₃ O ₅ | 5-Nitro-2-furfurylideneamino | H | H | H | H | 254-255 (MeNO ₂) | 83 | 247, 346, 373 |
| C ₈ H ₉ N ₃ O ₅ | 5-Amino-2-furfurylideneamino | H | H | H | H | ... | 30 | 153 |
| C ₈ H ₁₂ NO ₂ Cl | ClCH ₂ CH ₂ | —CH ₂ — | Me | Me | Me | 64-68 | .. | 132 |
| C ₉ H ₁₀ N ₂ O ₄ S | <i>p</i> -H ₂ NC ₆ H ₄ SO ₂ | H | H | H | H | ... | .. | 272 |
| C ₉ H ₁₃ NO ₂ Cl ₂ | <i>i</i> -Pr | —CCl ₂ — | Me | Me | Me | 44-46, 96-98 (1.8) | .. | 132 |
| C ₉ H ₁₄ N ₂ O ₄ SP | (EtO) ₂ P(S)CH ₂ CH ₂ | H | H | H | H | 188-192 (0.005) | .. | 102 |
| C ₉ H ₁₄ NO ₅ Cl ₂ P | (EtO) ₂ P(O)C(=CCl ₂) | H | H | H | H | ... | .. | 446 |
| C ₉ H ₁₅ NO ₂ | <i>i</i> -Pr | —CH ₂ — | Me | Me | Me | 87-91 | .. | 132 |
| C ₁₀ H ₈ N ₄ O ₅ S |  | H | H | H | H | 173 (EtOH) | .. | 150 |
| C ₁₀ H ₁₀ NO ₃ Cl | H | H | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | H | ... | .. | 13 |
| C ₁₀ H ₁₀ NO ₃ Br | H | H | H | <i>p</i> -BrC ₆ H ₄ OCH ₂ | H | 151-152.5 | .. | 13 |
| C ₁₀ H ₁₁ NO ₂ | H | H | H | PhOCH ₂ | H | 120-121 | .. | 13 |
| C ₁₀ H ₁₅ NO ₂ | Me | —CH ₂ — | —(CH ₂) ₈ — | —(CH ₂) ₈ — | Me | 76-78 | .. | 132 |
| C ₁₀ H ₁₅ NO ₂ Cl ₂ | Bu | —CCl ₂ — | Me | Me | Me | 32-38, 118-120 (1) | .. | 132 |
| C ₁₀ H ₁₇ NO ₂ | Bu | —CH ₂ — | Me | Me | Me | 112-114 (1) | .. | 132 |
| C ₁₀ H ₁₉ NO ₂ S | CH ₃ (CH ₂) ₄ SCH ₂ CH ₂ | H | H | H | H | 134-136 (0.1) | 96 | 239 |
| C ₁₁ H ₁₂ NO ₃ Cl | H | H | H | <i>o</i> -ClC ₆ H ₄ OCH ₂ | Me | 135-137 | .. | 13 |
| C ₁₁ H ₁₃ NO ₃ | H | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | H | 120-122 | .. | 13 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | PhOCH ₂ | Me | 112.5-114 | .. | 13 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | <i>m</i> -MeOC ₆ H ₄ OCH ₂ | H | 121-123 | .. | 13 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | <i>p</i> -MeOC ₆ H ₄ OCH ₂ | H | 103.5 | .. | 13 |
| C ₁₁ H ₁₃ NO ₄ | H | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 139-141 | .. | 13 |
| C ₁₁ H ₁₃ NO ₅ S | H | <i>p</i> -MeC ₆ H ₄ SO ₂ OCH ₂ | H | H | H | ... | .. | 13 |
| C ₁₁ H ₁₅ NO ₂ Cl ₂ | Bu | —CCl ₂ — | Et | Et | Me | 117-119 (0.6) | .. | 132 |
| C ₁₂ H ₁₂ NO ₃ Cl ₂ | 2,4,5-Cl ₃ C ₆ H ₂ OCH ₂ CH ₂ | H | H | Me | H | 76-79 | 13 | 239 |
| C ₁₂ H ₁₂ NO ₃ Cl ₂ | 2,4-Cl ₂ C ₆ H ₃ OCH ₂ CH ₂ | H | H | Me | H | 200 (0.1) | 60 | 239 |
| C ₁₂ H ₁₂ NO ₃ Cl ₂ | 3,4-Cl ₂ C ₆ H ₃ OCH ₂ CH ₂ | H | H | Me | H | 188-208 (0.3) | 31 | 239 |
| C ₁₂ H ₁₄ NO ₂ ClS | <i>p</i> -ClC ₆ H ₄ SCH ₂ CH ₂ | H | H | Me | H | ... | 96 | 239 |
| C ₁₂ H ₁₅ NO ₃ | PhOCH ₂ CH ₂ | H | H | Me | H | ... | 50 | 239 |
| C ₁₂ H ₁₅ NO ₄ | H | H | H | <i>o</i> -MeC ₆ H ₄ OCH ₂ | Me | 99-101 | .. | 13 |
| C ₁₂ H ₁₅ NO ₄ | H | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | Me | 88-90 | .. | 13 |
| C ₁₂ H ₁₅ NO ₄ | Me | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 72.5-75.0 | .. | 13 |
| C ₁₂ H ₁₅ NO ₅ S | H | <i>p</i> -MeC ₆ H ₄ SO ₂ OCH ₂ | Me | H | H | ... | .. | 13 |
| C ₁₂ H ₁₇ NO ₂ Cl ₂ | <i>i</i> -Pr | —CCl ₂ — | —(CH ₂) ₈ — | —(CH ₂) ₈ — | H | 155-157 | .. | 132 |
| C ₁₃ H ₁₀ NO ₆ |  | H | H | H | H | >300 | .. | 152 |
| C ₁₃ H ₁₇ NO ₃ | H | H | H | <i>p</i> - <i>i</i> -PrC ₆ H ₄ OCH ₂ | H | 120-122 | .. | 13 |
| C ₁₃ H ₁₇ NO ₄ | Et | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | 175-178 (0.1) | .. | 13 |
| C ₁₃ H ₁₇ NO ₄ | H | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | Et | ... | .. | 13 |
| C ₁₃ H ₁₇ NO ₅ S | H | <i>p</i> -MeC ₆ H ₄ SO ₂ OCH ₂ | Et | H | H | ... | .. | 13 |
| C ₁₃ H ₂₀ N ₂ O ₄ | Me ₂ N(CH ₂) ₂ OCO | Me | H | Ph | H | (<i>dl</i> - <i>cis</i>) 54 | .. | 303 |
| C ₁₇ H ₂₂ N ₂ O ₄ | Me ₂ N(CH ₂) ₄ OCO | Me | H | Ph | H | (<i>dl</i> - <i>trans</i> , HCl salt) 167 | .. | 303 |
| C ₁₈ H ₁₉ NO ₄ | PhCH ₂ | H | H | <i>o</i> -MeOC ₆ H ₄ OCH ₂ | H | (<i>dl</i> - <i>cis</i> , HCl salt) 151 | .. | 303 |
| C ₁₈ H ₁₉ NO ₅ S | CH ₃ (CH ₂) ₄ SCH ₂ CH ₂ | H | H | Me | H | 57-58 | .. | 13 |
| C ₁₈ H ₁₉ NO ₅ S | Structure or name | | | | | 180-200 (0.1) | 84 | 239 |
| |  | | | | | | | 476 |
| | Poly(N-allyl-5-methyl-2-oxazolidone) | | | | | 115 | .. | 539 |
| | Compounds of the following type of uncertain structure | | | | | | | 240 |
| |  | | | | | | | |

well as the usefulness of the drug against ornithosis (113), typhoid (92, 313), Salmonella-type infections (47, 72, 298, 416, 454, 475), leucocytozoon infection (6), and respiratory diseases in fowl (400). Its effectiveness in the control of trypanosoma infection in mice (70), furunculosis in trout (428-430), treatment

of hog plague virus (192), influence on the growth of pigs (432, 554), and control of pathogenic microorganisms in animals (281) has been studied. It is reported to be efficacious in infectious synovitis (473, 474), coccidiosis infections (33, 67, 343), trichomonas infections (253, 447, 493), and paratyphoid infections

(8). It is reported to be effective when included in animal feeds (14, 16, 552), as a nutritive preparation for fish breeding (268), as an antibacterial (9, 243, 254, 330, 603, 604), as an inhibitor of the growth of *Histomonas meleagridis* (252), to prevent pregnancy in mice (267), and to treat infectious putrefactive diseases in bees (378). Its effect on the excretion of B vitamins in the urine (266) has been studied. It has been suggested as a radioprotectant drug in man (220), for treating gastroenteritis in nursing infants (145), and for the therapy of lambliasis (62).

Many of these studies deal with Furazolidone in combination with other drugs; some deal with comparative studies (128). Since this substance is of such importance, many methods for producing it have been used. These have been treated in the appropriate sections dealing with the preparation of 2-oxazolidones. Additionally, there have been several studies that deal with the manufacturing aspects of producing Furazolidone, rather than with the chemical aspects (246, 451, 525).

2. *Furaltadone*

N-(5-nitro-2-furfurylidene)-3-amino-5(N-morpholinomethyl)-2-oxazolidone is known as Furaltadone or Furoxone. Though it has not been studied as extensively as Furazolidone, Furaltadone has been proposed as an antibacterial (73, 271, 469, 556, 605), and, more specifically, against staphylococcus infections (186, 287, 288, 390). Its effectiveness against mastitis (17, 436) and as an enzyme inhibitor (115) has been studied. Its influence on gastric secretion (355), facility of placental transfer (77), pharmacological properties (124, 337), distribution in the rat (76), and its value as a food additive (15) have been investigated. There has been a critical evaluation of the clinical and laboratory studies of Furaltadone (336) and several papers dealing with its manufacture (302, 490, 521).

3. *Methoxadone*

While the two substances discussed above find their major uses in controlling infection, 5-(*o*-methoxyphenoxy-methyl)-2-oxazolidone, or Methoxadone or Mephenoxalone, is used as a psychopharmacological (187) or neuropharmacological (208) compound. Its toxicity (51, 601), pharmacological activity (89, 95, 349, 601), metabolic fate (356), adrenolytic action (2), synergistic action with morphine, codeine, and the like (174), effect on reproduction (500), and its effect on blood pressure and behavioral responses (3) have been studied.

4. *Other Substances*

The medicinal properties of a number of other derivatives of 2-oxazolidone have been studied. Their anti-

bacterial (1, 45, 68, 71, 83, 86, 151, 168, 203, 242, 293, 301, 354, 423, 443, 444, 506, 557, 566, 572, 593), antimicrobial (10, 142, 197, 199, 200, 388, 391, 402, 418, 572), antiseptic (206), antibiotic (20, 63, 94, 234), antimetabolic (52, 88), antimitotic (546, 547), anti-anthelmintic (151, 239, 241, 242, 576), antiinflammatory (303), antipyretic (4, 20, 518), anticonvulsant (20, 97, 319, 324), and antiprotozoal (175) activities have been studied. Their effect on reproduction (411), toxicity (401, 405), vasomotor effects (82), lymphatic transport (78), metabolic degradation (292, 409), and excretion (416) have been reported. They have been suggested as chemotherapeutic agents (347, 414, 435), as growth promoters (53, 207, 408), as skeletal muscle relaxants (318, 322, 323, 350), as hypotensives (155), and as effective against organisms causing enterocolitis (294), *Trichomonas vaginalis* (450), pig ascarides (487), and hepatic cirrhosis (449). They have been found to have analgesic activity (20, 175, 303, 518), to inhibit swelling (43), and to serve as central nervous system relaxants (300, 335), central nervous system depressants (108, 320), vasoconstrictors (527), tranquilizers (12), and strychnine antagonists (321).

They have been suggested as fungicides (131, 132, 239, 241, 242, 468), insecticides (102, 112, 132, 239, 241, 242), herbicides (132, 133, 239, 438, 468, 487, 595), parasiticides (150, 576), nematocides (239, 468), and germicides (213, 275). They have been found effective in plant growth retardation (456, 582), as defoliating agents (61, 311), and as growth stimulants (58, 64).

B. POLYMERS

Derivatives of 2-oxazolidone have been polymerized (11, 24, 39, 40, 125-127, 139, 140, 143, 144, 146, 149, 158, 222, 237, 289, 291, 394, 460, 485, 489, 494, 519, 537, 539, 440, 542, 570, 571, 577, 578, 580, 583-585, 587, 594, 596, 597) and copolymerized (25, 26, 65, 91, 129, 131, 138, 188, 228, 229, 238, 270, 291, 348, 352, 360-365, 412, 467, 488, 499, 517, 538, 569, 574, 577, 579). In this connection, two studies report reactivity ratios for copolymers containing 2-oxazolidone derivatives (65, 229).

The polymers have been suggested for many uses: fibers (362, 365), tablet coatings (270, 519, 594), lubricant additives (91, 180, 291), cigarette filters (488, 537), ore clarification (517), rust inhibition (131), as components of photographic emulsions (125, 127, 146, 289), drilling muds (129), and hydraulic cements (569), as dye assistants for textiles (139, 158, 585), as dye-stripping compositions (539, 583), in the prevention of interfilamentary sticking (489) and bleeding of dyes (584), in hair-setting compositions (542), in propellants (540), in beverage clarification (539, 578), as water-soluble polymers (11, 140, 237, 580), in emulsification of silicone oils (348), and in preparations of thermoplastic foams (494).

C. MISCELLANEOUS

Derivatives of 2-oxazolidone have been suggested for the following uses: blowing agents (460), paper impregnation (596), extraction of hydrocarbons (387, 446, 496), solvents for polymers (311, 581), plasticizers (20, 81, 134, 239, 398), beverage clarification (162), metal coating (439), corrosion inhibition (133, 535), emulsifiers (239), bleaches (572), flame retarders (112), crease-resistance in textiles (112, 232), antistatic treatment of fibers (555), dyeing aids (137, 399, 602), laundering aids (568), waterproofing for textiles (551), sulfonation reagents (480), nitrating reagents (249), source of polyethylene polyamine (394), formation of polyester amides (392), and as a monoamine oxidase inhibitor (282).

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VIII. REFERENCES

- (1) ABIC Chemical Laboratories Ltd., Belgian Patent 624,402 (May 6, 1963); *Chem. Abstr.*, **60**, 8040 (1964).
- (2) Abitbol, H., Cabut, M. S., Guevara, R. O., and Grillo, S. A., *Rev. Soc. Agr. Biol.*, **38**, 253 (1962); *Chem. Abstr.*, **61**, 936 (1964).
- (3) Aceto, M. D. G., Kinnard, W. J., and Buckley, J. P., *Arch. Intern. Pharmacodyn.*, **144**, 214 (1963).
- (4) Adams, R., and Segur, J. B., *Science*, **52**, 185 (1920).
- (5) Adams, R., and Segur, J. B., *J. Am. Chem. Soc.*, **45**, 785 (1923).
- (6) Akiba, K., Morii, T., Ebisawa, S., Nozawa, S., and Minai, T., *Natl. Inst. Animal Health Quart.*, **3**, 188 (1963); *Chem. Abstr.*, **61**, 2234 (1964).
- (7) Alberti, C. G., Bernardi, L., Lavini, G., and Vercellone, A., *Farmaco (Pavia), Ed. Sci.*, **10**, 312 (1955); *Chem. Abstr.*, **50**, 3289 (1956).
- (8) Alekseeva, L., *Latvijas PSR Zinatnu Akad. Vestis*, **85** (1961); *Chem. Abstr.*, **56**, 16105 (1962).
- (9) Alekseeva, L. N., *Furezolidon, Akad. Nauk Latv. SSR, Inst. Organ. Sintezā*, **29** (1962); *Chem. Abstr.*, **59**, 15826 (1963).
- (10) Alekseeva, L., *Latvijas PSR Zinatnu Akad. Vestis*, **108** (1961); *Chem. Abstr.*, **55**, 23804 (1961).
- (11) Amende, J., and Kawka, E., German Patent 1,056,120 (April 30, 1959); *Chem. Abstr.*, **55**, 10391 (1961).
- (12) American Cyanamid Co., British Patent 894,198 (April 18, 1962); *Chem. Abstr.*, **59**, 633 (1963).
- (13) American Cyanamid Co., British Patent 938,424 (Oct 2, 1963); *Chem. Abstr.*, **60**, 4153 (1964).
- (14) Anon., *Federal Register*, **27**, 5430 (June 8, 1962); *Chem. Abstr.*, **57**, 6381 (1962).
- (15) Anon., *Federal Register*, **27**, 8307 (Aug 21, 1962); *Chem. Abstr.*, **57**, 12936 (1962).
- (16) Anon., *Federal Register*, **28**, 12665 (Nov 28, 1963); *Chem. Abstr.*, **60**, 4689 (1964).
- (17) Anon., *Federal Register*, **29**, 1459 (Jan 29, 1964); *Chem. Abstr.*, **60**, 9820 (1964).
- (18) Anon., *J. Assoc. Offic. Agr. Chemists*, **40**, 39 (1957); *Chem. Abstr.*, **51**, 4867 (1957).
- (19) Anon., *J. Assoc. Offic. Agr. Chemists*, **41**, 31 (1958); *Chem. Abstr.*, **52**, 6051 (1958).
- (20) Applegath, F., and Franz, R. A., U. S. Patent 2,857,392 (Oct 21, 1958); *Chem. Abstr.*, **53**, 5286 (1959).
- (21) Arcus, C. L., and Greenwood, D. B., *J. Chem. Soc.*, 1937 (1953).
- (22) Ardis, A. E., Baltzly, R., and Schoen, W., *J. Am. Chem. Soc.*, **68**, 591 (1946).
- (23) Arend, W., and Trieschmann, H. G., German Patent 972,304 (July 2, 1959); *Chem. Abstr.*, **55**, 5531 (1961).
- (24) Armen, A., and Ehlers, F. A., U. S. Patent 3,057,816 (Oct 9, 1962); *Chem. Abstr.*, **58**, 1561 (1963).
- (25) Armen, A., and Murdock, S. A., U. S. Patent 3,083,177 (March 26, 1963); *Chem. Abstr.*, **58**, 14218 (1963).
- (26) Arnesen, F. M., and Cloninger, L. C., U. S. Patent 3,035,010 (May 15, 1962); *Chem. Abstr.*, **57**, 8754 (1962).
- (27) Arnold, H., and Bekel, H., French Patent 1,345,001 (Dec 6, 1963); *Chem. Abstr.*, **61**, 7020 (1964).
- (28) Arnold, H., and Bekel, H., *Arzneimittel-Forsch.*, **14**, 750 (1964); *Chem. Abstr.*, **62**, 428 (1965).
- (29) Asahi, Y., *Takeda Kenkyusho Nempo*, **19**, 31 (1960); *Chem. Abstr.*, **55**, 13132 (1961).
- (30) Ash, A. S. F., Creighton, A. M., and Wragg, W. R., British Patent 971,041 (Sept 30, 1964); *Chem. Abstr.*, **61**, 14692 (1964).
- (31) Asta-Werke Akt.-Ges., Chemische Fabrik, Dutch Patent Appl. 6,410,202 (March 15, 1965); *Chem. Abstr.*, **63**, 11572 (1965).
- (32) Auge, J. A. B., and Tayade, S. M. E., Spanish Patent 257,459 (April 8, 1960); *Chem. Abstr.*, **56**, 5970 (1962).
- (33) Aycardi, J., *Ann. Inst. Natl. Rech. Agron., Ser. D*, **9**, 217 (1960); *Chem. Abstr.*, **55**, 8671 (1963).
- (34) Badische Anilin- und Soda-Fabrik, Akt.-Ges., British Patent 728,699 (April 27, 1955); *Chem. Abstr.*, **50**, 6521 (1956).
- (35) Baiocchi, F., Franz, R. A., and Horwitz, L., *J. Org. Chem.*, **21**, 1546 (1956).
- (36) Baizer, M. M., U. S. Patent 3,168,525 (Feb 2, 1965); *Chem. Abstr.*, **62**, 16253 (1965).
- (37) Baker, W., and Ollis, W. D., *J. Chem. Soc.*, 556 (1951).
- (38) Bakke, W. W., U. S. Patent 2,905,690 (Sept 22, 1959); *Chem. Abstr.*, **54**, 5698 (1960).
- (39) Bakke, W. W., U. S. Patent 3,033,829 (May 8, 1962); *Chem. Abstr.*, **57**, 7471 (1962).
- (40) Bakke, W. W., Walles, W. E., and Tousignant, W. F., U. S. Patent 2,993,031 (July 18, 1961); *Chem. Abstr.*, **55**, 24107 (1961).
- (41) Baltzly, R., and Buck, J. S., *J. Am. Chem. Soc.*, **62**, 164 (1940).
- (42) Beachell, H. C., and NgocSon, C. P., *J. Polymer Sci.*, **A2**, 4773 (1964).
- (43) Beale, A. F., Jr., U. S. Patent 3,179,171 (April 20, 1965); *Chem. Abstr.*, **62**, 15967 (1965).
- (44) Beasley, Y. M., Petrow, V., Stephenson, O., and Thomas, A. J., *J. Pharm. Pharmacol.*, **9**, 10 (1957); *Chem. Abstr.*, **51**, 8723 (1957).
- (45) Beckett, A. H., and Robinson, A. E., *J. Med. Pharm. Chem.*, **1**, 155 (1959); *Chem. Abstr.*, **53**, 20242 (1959).
- (46) Beckman, H. F., *J. Agr. Food Chem.*, **6**, 130 (1958).
- (47) Belding, R. C., and Mayer, M. L., *Poultry Sci.*, **37**, 459 (1958); *Chem. Abstr.*, **53**, 1537 (1959).
- (48) Bell, J. B., Jr., and Malkemus, J. D., U. S. Patent 2,755,286 (July 17, 1956); *Chem. Abstr.*, **51**, 2871 (1957).
- (49) Belloff, G. B., Buzard, J., and Roberts, H. D. B., *Poultry Sci.*, **37**, 223 (1958); *Chem. Abstr.*, **53**, 1537 (1958).
- (50) Ben-Ishai, D., *J. Am. Chem. Soc.*, **78**, 4962 (1956).
- (51) Benitz, K. F., Moraski, R., Roepke, R. R., and Wozniak,

- L. A., *Toxicol. Appl. Pharmacol.*, **4**, 220 (1962); *Chem. Abstr.*, **56**, 14577 (1962).
- (52) Berenblum, I., Ben-Ishai, D., Haron-Cheva, N., Lapidot, A., Simon, E., and Trainin, N., *Biochem. Pharmacol.*, **2**, 168 (1959); *Chem. Abstr.*, **54**, 23055 (1960).
- (53) Berg, L. R., Hamilton, C. M., and Bearse, G. E., *Poultry Sci.*, **35**, 1394 (1956); *Chem. Abstr.*, **51**, 15772 (1957).
- (54) Bergmann, E. D., *Chem. Rev.*, **53**, 309 (1953).
- (55) Bergmann, E. D., and Sulzbacher, M., *J. Org. Chem.*, **16**, 84 (1951).
- (56) Berlin, A. Y., and Yaguzhinskii, L. S., *Puti Sintezy i Izyskaniya Protiwoopukholyevykh Preparatov, Tr. Simpoziuma po Khim. Protiwoopukholyevykh Veshchestv, Moscow, 1960*, 92 (1962); *Chem. Abstr.*, **58**, 6822 (1963).
- (57) Bimber, R. M., U. S. Patent 2,973,366 (Feb 28, 1961); *Chem. Abstr.*, **55**, 17653 (1961).
- (58) Bindler, J., and Rumpf, J. A., Swiss Patent 360,843 (April 30, 1962); *Chem. Abstr.*, **58**, 9576 (1963).
- (59) Blajot, I. B., and Corominas, J. P., Spanish Patent 239,904 (Feb 20, 1958); *Chem. Abstr.*, **54**, 12159 (1960).
- (60) Blomquist, A. T., and Fiedorek, F. T., U. S. Patent 2,485,855 (Oct 25, 1949); *Chem. Abstr.*, **44**, 3516 (1950).
- (61) Bluestone, H., U. S. Patent 2,860,043 (Nov. 11, 1958); *Chem. Abstr.*, **54**, 1798 (1960).
- (62) Blugers, A., Hillers, S., and Shenigson, B. S., *Med. Parazitol. i Parazitan. Bolezni*, **29**, 646 (1960); *Chem. Abstr.*, **55**, 16820 (1961).
- (63) Blugers, A., Stradins, J., Dzene, A., and Tiltins, M., *Urologiya*, **26**, 52 (1961); *Chem. Abstr.*, **56**, 5339 (1962).
- (64) Boileau, J., Faidutti, M., Konrat, J. P., and Billaz, R., French Patent 1,358,627 (April 17, 1964); *Chem. Abstr.*, **61**, 9975 (1964).
- (65) Bork, J. F., and Coleman, L. E., *J. Polymer Sci.*, **43**, 413 (1960).
- (66) Boucherle, A., Carraz, G., and Bonnin, J., *Bull. Soc. Chim. France*, 231 (1958).
- (67) Boyer, C. I., and Brown, J., *Rept. N. Y. State Vet. Coll., Cornell Univ., 1952-1953*, 31 (1954); *Chem. Abstr.*, **48**, 12320 (1954).
- (68) Bravard, L. E., British Patent 788,373 (Jan 2, 1958); *Chem. Abstr.*, **52**, 12935 (1958).
- (69) Breinlich, J., *Deut. Apotheker-Ztg.*, **104**, 534 (1964); *Chem. Abstr.*, **61**, 5459 (1964).
- (70) Brener, Z., *Hospital*, **60**, 947 (1961); *Chem. Abstr.*, **56**, 16092 (1962).
- (71) Buckett, W. R., and Kidd, D., *J. Pharm. Pharmacol.*, **16**, 663 (1964); *Chem. Abstr.*, **61**, 16062 (1964).
- (72) Buiké, A., *Latvijas Lopkopibas un Vet. Zinatniski Peticiskais Inst. Raksti*, **15**, 75 (1963); *Chem. Abstr.*, **61**, 9799 (1964).
- (73) Burdin, J. C., Perchebois, G., Delagoutte, A. P., and Mauuary, G., *Ann. Med. Nancy*, **3**, 110 (1964); *Chem. Abstr.*, **61**, 7402 (1964).
- (74) Burkett, H., Nelson, G., and Wright, W., *J. Am. Chem. Soc.*, **80**, 5812 (1958).
- (75) Burr, J. G., *J. Am. Chem. Soc.*, **75**, 1990 (1953).
- (76) Buzard, J. A., and Conklin, J. D., *Antibiot. Chemotherapy*, **11**, 89 (1961); *Chem. Abstr.*, **55**, 26244 (1961).
- (77) Buzard, J. A., and Conklin, J. D., *Am. J. Physiol.*, **206**, 189 (1964); *Chem. Abstr.*, **60**, 11242 (1964).
- (78) Buzard, J. A., Conklin, J. D., and Buller, R. H., *Am. J. Physiol.*, **201**, 492 (1961); *Chem. Abstr.*, **56**, 1943 (1962).
- (79) Buzard, J. A., Ells, V. R., and Paul, M. F., *J. Assoc. Offic. Agr. Chemists*, **39**, 512 (1956); *Chem. Abstr.*, **51**, 1502 (1957).
- (80) Buzard, J. A., Vrablic, D. M., and Paul, M. F., *Antibiot. Chemotherapy*, **6**, 702 (1956); *Chem. Abstr.*, **51**, 14872 (1957).
- (81) Caldwell, J. R., U. S. Patent 2,656,328 (Oct 20, 1953); *Chem. Abstr.*, **48**, 2415 (1954).
- (82) Calesnick, B., *Antibiot. Ann., 1958-1959*, 75 (1959); *Chem. Abstr.*, **54**, 11295 (1960).
- (83) Cameron, M. D., U. S. Patent 2,844,590 (July 22, 1958); *Chem. Abstr.*, **53**, 2254 (1959).
- (84) Cantor, A., and Winicov, M. W., Belgian Patent 630,409 (Oct 21, 1963); *Chem. Abstr.*, **60**, 15689 (1964).
- (85) Caradonna, C., and Stein, M. L., *Ann. Chim. (Rome)*, **54**, 539 (1964); *Chem. Abstr.*, **61**, 8292 (1964).
- (86) Carey, W. F., Russell, E. H., and O'Connor, J. R., *Antimicrobial Agents Ann.*, 152 (1960); *Chem. Abstr.*, **56**, 13345 (1962).
- (87) Carlson, C. W., and Wilcox, R. A., *Proc. S. Dakota Acad. Sci.*, **38**, 133 (1959); *Chem. Abstr.*, **54**, 13298 (1960).
- (88) Carraz, G., and Boucherle, A., *Thérapie*, **13**, 1063 (1958); *Chem. Abstr.*, **55**, 2822 (1961).
- (89) Carroll, M. N., Jr., Lutten, W. R., and Southward, R. W., *Arch. Intern. Pharmacodyn.*, **130**, 280 (1961); *Chem. Abstr.*, **55**, 20184 (1961).
- (90) Cason, J., and Prout, F. S., *J. Am. Chem. Soc.*, **71**, 1218 (1949).
- (91) Castrol Ltd., French Patent 1,366,096 (July 10, 1964); *Chem. Abstr.*, **61**, 15915 (1964).
- (92) Chakraborty, G., *Indian J. Pediat.*, **28**, 357 (1964); *Chem. Abstr.*, **61**, 11224 (1964).
- (93) Chauveau, A., Verny, E., and Verney, P., French Patent 1,271,038 (Jan 8, 1962); *Chem. Abstr.*, **56**, 15485 (1962).
- (94) Chernomordik, A. B., Kovalenko, A. D., and Andreenko, L. M., *Antibiotiki*, **6**, 735 (1961); *Chem. Abstr.*, **57**, 13005 (1962).
- (95) Cheymol, J., and Bourillet, F., *Ann. Pharm. Franc.*, **13**, 569 (1955); *Chem. Abstr.*, **50**, 11316 (1956).
- (96) Close, W. J., *J. Org. Chem.*, **15**, 1131 (1950).
- (97) Close, W. J., *J. Am. Chem. Soc.*, **73**, 95 (1951).
- (98) Coates, M. E., and Harrison, G. F., *Brit. J. Nutrition*, **13**, 345 (1959); *Chem. Abstr.*, **54**, 5849 (1960).
- (99) Cockburn, W. F., and McKay, A. F., *J. Org. Chem.*, **18**, 316 (1953).
- (100) Coll, A. L. P., Spanish Patent 288,893 (Oct 3, 1964); *Chem. Abstr.*, **61**, 1831 (1964).
- (101) Coll, A. L. P., and Coll, A. P., Spanish Patent 254,850 (Jan 12, 1960); *Chem. Abstr.*, **55**, 24790 (1961).
- (102) Cooper, McDougall and Robertson Ltd., Belgian Patent 633,832 (Dec 19, 1963); *Chem. Abstr.*, **61**, 13315 (1964).
- (103) Cooper, D. M., and Skulski, G., *J. Comp. Pathol. Therap.*, **66**, 299 (1956); *Chem. Abstr.*, **51**, 5929 (1957).
- (104) Cornforth, J. W., in "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, pp 396-402.
- (105) Corominas, J. P., and Lauger, M., *Helv. Chim. Acta*, **43**, 1862 (1960).
- (106) Cox, P. L., and Heotis, J. P., *J. Agr. Food Chem.*, **11**, 499 (1963).
- (107) Craig, W. C., and Henze, H. R., *J. Org. Chem.*, **10**, 16 (1945).
- (108) Crescenzi, E., Uberti, E. M., and Donini, F., *Farmaco, Ed. Sci.*, **20**, 159 (1965); *Chem. Abstr.*, **62**, 14645 (1965).
- (109) Crowther, H. L., and McCombie, H., *J. Chem. Soc.*, **103**, 27 (1913).
- (110) Crowther, M., and Nummy, W. R., U. S. Patent 2,806,839 (Sept 17, 1957); *Chem. Abstr.*, **52**, 3405 (1958).
- (111) Cummins, R. W., *J. Org. Chem.*, **28**, 85 (1963).
- (112) Davies, J. J., and Wallis, W. E., U. S. Patent 3,149,121 (Sept 15, 1964); *Chem. Abstr.*, **61**, 13313 (1964).

- (113) Davis, D. E., *Southwestern Vet.*, **11**, 29 (1957); *Chem. Abstr.*, **52**, 10403 (1958).
- (114) Dean, W. F., and Stephenson, E. L., *Poultry Sci.*, **37**, 124 (1958); *Chem. Abstr.*, **53**, 1480 (1959).
- (115) Dietrich, R. A., and Helleman, L., *J. Biol. Chem.*, **238**, 1683 (1963).
- (116) Delaby, R., Brustlein, F., Warolin, C., and Chabrier, P., *Bull. Soc. Chim. France*, 2056 (1961).
- (117) Delaby, R., Chabrier, P., and Najer, H., *Compt. Rend.*, **235**, 1131 (1952); *Chem. Abstr.*, **47**, 10525 (1953).
- (118) Delaby, R., and Damiens, R., *Festschr. Arthur Stoll*, 474 (1957); *Chem. Abstr.*, **53**, 376 (1959).
- (119) Delaby, R., Damiens, R., and Capmau, M. L., *Compt. Rend.*, **246**, 5 (1958); *Chem. Abstr.*, **53**, 9055 (1959).
- (120) Delaby, R., Damiens, R., and d'Huyt za, G., *Compt. Rend.*, **236**, 2076 (1953); *Chem. Abstr.*, **48**, 5111 (1954).
- (121) Delaby, R., Damiens, R., and d'Huyt za, G., *Ann. Pharm. Franc.*, **13**, 565 (1955); *Chem. Abstr.*, **50**, 11316 (1956).
- (122) Delaby, R., Damiens, R., and d'Huyt za, G., *Bull. Soc. Chim. France*, 831 (1956).
- (123) Delaby, R., Warolin, C., and Brustlein, F., *Compt. Rend.*, **237**, 1714 (1954); *Chem. Abstr.*, **49**, 8923 (1955).
- (124) Della Bella, D., Rognoni, F., and Verga, G., *Gior. Ital. Chemioterap.*, 5-9, 13 (1962); *Chem. Abstr.*, **57**, 15757 (1962).
- (125) Dersch, F., Belgian Patent 612,836 (Feb 15, 1962); *Chem. Abstr.*, **57**, 13334 (1962).
- (126) Dersch, F., and De Angelus, M. R., U. S. Patent 3,006,760 (Appl. Oct. 23, 1958); *Chem. Abstr.*, **56**, 2104 (1962).
- (127) Dersch, F., and DeAngelus, M. R., U. S. Patent 3,006,762 (Appl. Feb 9, 1959); *Chem. Abstr.*, **56**, 2104 (1962).
- (128) Dessi, P., and Murari, G., *Boll. Soc. Ital. Biol. Sper.*, **37**, 761 (1961); *Chem. Abstr.*, **56**, 1955 (1962).
- (129) Dever, C. D., and Ryan, R. F., U. S. Patent 3,108,956 (Oct 29, 1963); *Chem. Abstr.*, **60**, 1519 (1964).
- (130) Dillon, J. F., *World's Poultry Congr. Proc.*, 12th, Sydney, 1962, 157 (1962); *Chem. Abstr.*, **58**, 11736 (1963).
- (131) Dimroth, P., and Pasedach, H., German Patent 1,164,411 (March 5, 1964); *Chem. Abstr.*, **60**, 14510 (1964).
- (132) Dimroth, P., and Pasedach, H., German Patent 1,190,943 (April 15, 1965); *Chem. Abstr.*, **63**, 8366 (1965).
- (133) Dimroth, P., Pasedach, H., and Schefczik, E., German Patent 1,151,507 (July 18, 1963); *Chem. Abstr.*, **60**, 2934 (1964).
- (134) Dixon, S., U. S. Patent 2,977,371 (March 28, 1961); *Chem. Abstr.*, **55**, 17652 (1961).
- (135) Dixon, S., and Verbanc, J. J., U. S. Patent 2,977,369 (March 28, 1961); *Chem. Abstr.*, **55**, 17652 (1961).
- (136) Dougherty, E., 3rd, *Rept. N. Y. State Vet. Coll., Cornell Univ., 1956-1957*, 34 (1957); *Chem. Abstr.*, **52**, 16615 (1958).
- (137) Dow Chemical Co., British Patent 829,075 (Feb 24, 1960); *Chem. Abstr.*, **54**, 13677 (1960).
- (138) Dow Chemical Co., British Patent 896,456 (May 16, 1962); *Chem. Abstr.*, **57**, 4887 (1962).
- (139) Dow Chemical Co., British Patent 922,672 (April 3, 1963); *Chem. Abstr.*, **60**, 16047 (1964).
- (140) Dow Chemical Co., French Patent 1,331,404 (July 5, 1963); *Chem. Abstr.*, **59**, 12986 (1963).
- (141) Drake, G. D., Gever, G., and Hayes, K. J., U. S. Patent 2,740,792 (April 3, 1956); *Chem. Abstr.*, **51**, 1288 (1957).
- (142) Drake, G. D., and Hayes, K. J., U. S. Patent 2,759,931 (Aug 31, 1956); *Chem. Abstr.*, **51**, 2051 (1957).
- (143) Drechsel, E. K., *J. Org. Chem.*, **22**, 849 (1957).
- (144) Drechsel, E. K., U. S. Patent 2,818,362 and 2,818,399 (Dec 31, 1957); *Chem. Abstr.*, **52**, 5882 (1958).
- (145) Ducas, J., *Ann. Med. Nancy*, **2**, 1014 (1963); *Chem. Abstr.*, **60**, 6110 (1964).
- (146) DuPont de Nemours and Co., E. I., British Patent 867,899 (May 10, 1961); *Chem. Abstr.*, **55**, 21934 (1961).
- (147) Dyer, E., and Scott, H., *J. Am. Chem. Soc.*, **79**, 672 (1957).
- (148) Easton, N. R., Cassady, D. R., and Dillard, R. D., *J. Org. Chem.*, **27**, 2927 (1962).
- (149) Ebert, P. E., *Dissertation Abstr.*, **21**, 755 (1960); *Chem. Abstr.*, **55**, 8387 (1961).
- (150) Ebetino, F. F., Belgian Patent 614,686 (March 30, 1962); *Chem. Abstr.*, **58**, 529 (1963).
- (151) Ebetino, F. F., U. S. Patent 3,141,889 (July 21, 1964); *Chem. Abstr.*, **61**, 9502, (1964).
- (152) Ebetino, F. F., Carroll, J. J., and Gever, G., *J. Med. Pharm. Chem.*, **5**, 513 (1962); *Chem. Abstr.*, **57**, 9774 (1962).
- (153) Ebetino, F. F., and Gever, G., French Patent 1,334,109 (Aug 2, 1963); *Chem. Abstr.*, **61**, 4314 (1964).
- (154) Ebetino, F. F., Gever, G., and Hayes, K. J., U. S. Patent 2,759,932 (Aug 21, 1956); *Chem. Abstr.*, **51**, 2051 (1957).
- (155) Edlin, A. I., Buckley, J. P., Kinnard, W. J., and Aceto, M. D., *Arch. Intern. Pharmacodyn.*, **149**, 434 (1964); *Chem. Abstr.*, **61**, 9925 (1964).
- (156) Edwards, W. M., *Dissertation Abstr.*, **17**, 2810 (1957).
- (157) Egerts, V., Simanska, M., and Hillers, S., *Latvijas PSR Zinatnu Akad. Vestis, Kim. Ser.*, **2**, 199 (1961); *Chem. Abstr.*, **57**, 16749 (1962).
- (158) Ehlers, F. A., U. S. Patent 3,017,390 (Jan 16, 1962); *Chem. Abstr.*, **57**, 2460 (1962).
- (159) Eiduss, J., and Muceniece, L., *Latvijas PSR Zinatnu Akad. Vestis*, 65 (1961); *Chem. Abstr.*, **56**, 13680 (1962).
- (160) Eiduss, J., Venters, K., and Hillers, S., *Fiz. Probl. Spektroskopii, Akad. Nauk SSSR, Materialy 13-go (Trinadtsatogo) Soveshch., Leningrad, 1960*, **1**, 276 (1962); *Chem. Abstr.*, **59**, 10896 (1963).
- (161) Eiduss, Y. A., Venters, K., and Hillers, S., *Dokl. Akad. Nauk SSSR*, **141**, 655 (1961); *Chem. Abstr.*, **57**, 6755 (1962).
- (162) Elder, M. E., Moore, C., and Tousignant, W. F., U. S. Patent 3,146,107 (Aug 25, 1964); *Chem. Abstr.*, **61**, 16743 (1964).
- (163) Eloy, F., and Moussebois, C., *Bull. Soc. Chim. Belges*, **68**, 423 (1959); *Chem. Abstr.*, **54**, 7625 (1960).
- (164) Etlis, V. S., Sineokov, A. P., and Razuvaev, G. A., *Zh. Obshch. Khim.*, **34**, 4018 (1964); *Chem. Abstr.*, **62**, 9132 (1965).
- (165) Etlis, V. S., Sineokov, A. P., and Razuvaev, G. A., *Zh. Obshch. Khim.*, **34**, 4090 (1964); *J. Gen. Chem. USSR*, **34**, 4149 (1964); *Chem. Abstr.*, **62**, 10423 (1965).
- (166) Ettl, V., and Weichet, J., *Collection Czech. Chem. Commun.*, **13**, 316 (1948); *Chem. Abstr.*, **42**, 8190 (1948).
- (167) Evans, R. F., and Jones, J. I., *Chem. Ind. (London)*, 915 (1958).
- (168) Failla, L., Massaroli, G., Scuri, R., and Signorelli, G., *Farmaco (Pavia), Ed. Sci.*, **19**, 269 (1964); *Chem. Abstr.*, **60**, 15851 (1964).
- (169) Feinauer, R., Jacobi, M., and Hamann, K., *Ber.*, **98**, 1782 (1965).
- (170) Feuer, L., Szoke, S., Somogyi, D., and Szentmiklossy, P., Hungarian Patent 150,281 (1963); *Chem. Abstr.*, **60**, 2935 (1964).
- (171) Fieser, L. F., and Fieser, M., "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, p 499 ff.
- (172) Fischer, E., *J. Chem. Soc.*, 4525 (1952).
- (173) Fischer, E., *J. Chem. Soc.*, 2836 (1953).

- (174) Fischer, E., Szabo, J. L. J., and Stamburg, M., *Nature*, **186**, 893 (1960); *Chem. Abstr.*, **55**, 4775 (1961).
- (175) Fischer, E., Szabo, J. L., and Stark, P. P., U. S. Patent 3,110,650 (Nov 12, 1963); *Chem. Abstr.*, **60**, 5287 (1964).
- (176) Fodor, G., and Koczka, K., *J. Chem. Soc.*, 850 (1952).
- (177) Formini, R. L., and Little, E. D., U. S. Patent 3,194,810 (July 13, 1965); *Chem. Abstr.*, **63**, 9946 (1965).
- (178) Francis, D. W., and Shaffner, C. S., *Poultry Sci.*, **35**, 1371 (1956); *Chem. Abstr.*, **51**, 15772 (1957).
- (179) Frazier, T. C., Little, E. D., and Lloyd, B. E., *J. Org. Chem.*, **25**, 1944 (1960).
- (180) Frew, D. W., Jr., U. S. Patent 3,146,203 (Aug 25, 1964); *Chem. Abstr.*, **61**, 14447 (1964).
- (181) Fricke, F. L., Keppel, G. E., and Hart, S. M., *J. Assoc. Agr. Chemists*, **47**, 788 (1964); *Chem. Abstr.*, **61**, 11251 (1964).
- (182) Fromm, E., and Honold, E., *Ber.*, **55B**, 902 (1922).
- (183) Fromm, E., *Ann.*, **467**, 240 (1928).
- (184) Fukui, K., and Kitano, H., Japanese Patent 11,837 (Aug 24, 1960); *Chem. Abstr.*, **55**, 10482 (1961).
- (185) Fuller, H. L., and Dunahoo, W. S., *Poultry Sci.*, **38**, 1150 (1959); *Chem. Abstr.*, **54**, 7886 (1960).
- (186) Fumagalli, E., *Gazz. Med. Ital.*, **120**, 245 (1961); *Chem. Abstr.*, **60**, 13098 (1964).
- (187) Furgiuele, A. R., Kinnard, W. J., and Buckley, J. P., *J. Pharm. Sci.*, **50**, 252 (1961); *Chem. Abstr.*, **55**, 13674 (1961).
- (188) Furukawa, J., Yamashita, S., and Okamoto, H., Japanese Patent 7146 (May 27, 1963); *Chem. Abstr.*, **60**, 16009 (1964).
- (189) Gabriel, S., *Ber.*, **21**, 566 (1888).
- (190) Gabriel, S., *Ber.*, **38**, 2405 (1905).
- (191) Gabriel, S., and Eschenbach, G., *Ber.*, **30**, 2494 (1897).
- (192) Gannushkin, M. S., Zablotskii, T. M., and Bessarabov, B. F., *Materialy 7-oi (Sed'moi), Nauchn. Konf. po Infekts. i Invazion. Zabolovaniyam Sel'skokhoz. Zhivotnykh. Moscow*, **3** (1961); *Chem. Abstr.*, **58**, 2763 (1963).
- (193) General Aniline and Film Corp., French Patent 1,354,115 (March 6, 1964); *Chem. Abstr.*, **61**, 5809 (1964).
- (194) Gentry, R. F., *Avian Diseases*, **2**, 76 (1958); *Chem. Abstr.*, **54**, 11261 (1960).
- (195) Gever, G., U. S. Patent 2,652,402 (Sept 15, 1953); *Chem. Abstr.*, **48**, 12179 (1954); German Patent 1,013,287 (Aug 8, 1957); *Chem. Abstr.*, **54**, 5698 (1960).
- (196) Gever, G., *J. Am. Chem. Soc.*, **76**, 1283 (1954).
- (197) Gever, G., U. S. Patent 2,695,300 (Nov 23, 1954); *Chem. Abstr.*, **49**, 15975 (1955).
- (198) Gever, G., U. S. Patent 2,695,300 (Nov 23, 1954); *Chem. Abstr.*, **49**, 15975 (1955).
- (199) Gever, G., U. S. Patent 2,798,068 (July 2, 1957); *Chem. Abstr.*, **52**, 443 (1958).
- (200) Gever, G., U. S. Patent 2,802,002 (Aug 6, 1957); *Chem. Abstr.*, **51**, 18007 (1957).
- (201) Gever, G., U. S. Patent 2,852,451 (Sept 16, 1958); *Chem. Abstr.*, **53**, 3243 (1959).
- (202) Gever, G., U. S. Patent 2,908,689 (Oct 13, 1959); *Chem. Abstr.*, **55**, 3618 (1961).
- (203) Gever, G., German Patent 1,126,877 (April 5, 1962); *Chem. Abstr.*, **58**, 4578 (1963).
- (204) Gever, G., and O'Keefe, C. J., U. S. Patent 2,927,110 (March 1, 1960); *Chem. Abstr.*, **54**, 12158 (1960).
- (205) Gever, G., O'Keefe, C., Drake, G., Ebetino, F., Michels, J., and Hayes, K., *J. Am. Chem. Soc.*, **77**, 2277 (1955).
- (206) Goda, M., and Isa, Y., *Nippon Suisan Gakkaishi*, **25**, 525 (1959); *Chem. Abstr.*, **54**, 18823 (1960).
- (207) Gotoh, J., and Sato, K., *World's Poultry Congr. Proc.*, **12th**, Sydney, 1960, 276 (1962); *Chem. Abstr.*, **58**, 11734 (1963).
- (208) Gray, W. D., Osterberg, A. C., and Rauh, C. E., *Arch. Intern. Pharmacodyn.*, **134**, 198 (1961).
- (209) Grewe, R., and Herberg, H. W., *Ber.*, **92**, 1195 (1959).
- (210) Gross, P. H., Brendel, K., and Zimmerman, H. K., *Angew. Chem.*, **76**, 377 (1964).
- (211) Gross, P. H., Brendel, K., and Zimmerman, H. K., *Ann.*, **680**, 159 (1964).
- (212) Gross, H. G., Brendel, K., and Zimmerman, H. K., *Ann.*, **681**, 225 (1965).
- (213) Grosser, F., and Susko, J., U. S. Patent 3,136,755 (June 1964); *Chem. Abstr.*, **61**, 5467 (1964).
- (214) Gulbins, K., Benzing, G., Maysenhölder, R., and Hamann, K., *Ber.*, **93**, 1975 (1960).
- (215) Gulbins, K., and Hamann, K., *Angew. Chem.*, **20**, 705 (1958).
- (216) Gulbins, K., and Hamann, K., German Patent 1,068,715 (Nov 12, 1959); *Chem. Abstr.*, **55**, 12424 (1961).
- (217) Gulbins, K., and Hamann, K., *Angew. Chem.*, **73**, 434 (1961).
- (218) Guth, D. C., and Schaefer, F. C., U. S. Patent 2,813,847 (Nov 19, 1957); *Chem. Abstr.*, **52**, 4245 (1958).
- (219) Haber, R. G., Israeli Patent 16,256 (May 25, 1963); *Chem. Abstr.*, **60**, 2957 (1964).
- (220) Haley, T. J., *Giorn. Ital. Chemioterap.*, **6-9**, 213 (1962); *Chem. Abstr.*, **58**, 12847 (1963).
- (221) Hall, H. K., Brandt, M. K., and Mason, R. M., *J. Am. Chem. Soc.*, **80**, 6420 (1958).
- (222) Hall, H. K., Jr., and Schneider, A. K., *J. Am. Chem. Soc.*, **80**, 6409 (1958).
- (223) Hall, H. K., Jr., and Zbinden, R., *J. Am. Chem. Soc.*, **80**, 6428 (1958).
- (224) Hamashima, Y., Tori, K., and Takamizawa, A., *Chem. Pharm. Bull.*, (Tokyo), **13**, 1052 (1965); *Chem. Abstr.*, **64**, 761 (1966).
- (225) Haraoka, Y., Sugihara, A., and Ito, M., Japanese Patent 10,147 (May 24, 1965); *Chem. Abstr.*, **63**, 5657 (1965).
- (226) Harrington, R. C., Jr., U. S. Patent 2,865,926 (Dec 23, 1958); *Chem. Abstr.*, **53**, 8164 (1959).
- (227) Harris, N. D., *J. Org. Chem.*, **28**, 745 (1963).
- (228) Hart, R., *Makromol. Chem.*, **47**, 143 (1961); *Chem. Abstr.*, **56**, 10387 (1962).
- (229) Hart, R., and Timmerman, D., *Makromol. Chem.*, **31**, 223 (1959); *Chem. Abstr.*, **53**, 19448 (1959).
- (230) Heathcock, C., and Hassner, A., *Angew. Chem.*, **75**, 344 (1963); *Angew. Chem. Intern. Ed. Engl.*, **2**, 213 (1963).
- (231) Hechelhammer, W., and Coenen, M., German Patent 839,037 (May 15, 1952); *Chem. Abstr.*, **51**, 14823 (1957).
- (232) Heinisch, E., and Hussong, M., Germany Patent 1,105,377 (April 27, 1961); *Chem. Abstr.*, **55**, 27911 (1961).
- (233) Hellinghuizer-Gerriesen, B., British Patents 862,206 and 862,207 (March 1, 1961); *Chem. Abstr.*, **55**, 15511 (1961).
- (234) Hellinghuizer-Gerriesen, B., British Patent 864,012 (May 29, 1961); *Chem. Abstr.*, **55**, 18774 (1961).
- (235) Hennion, G. F., and O'Shea, F. X., *J. Org. Chem.*, **23**, 662 (1958).
- (236) Herrett, R. J., and Buzard, J. A., *Anal. Chem.*, **32**, 1676 (1960).
- (237) Hibbard, B. B., British Patent 951,496 (May 4, 1964); *Chem. Abstr.*, **60**, 16005 (1964).
- (238) Hibbard, B. B., and Weage, D. D., U. S. Patent 3,044,992 (July 17, 1962); *Chem. Abstr.*, **57**, 12739 (1962).
- (239) Hickner, R. A., U. S. Patent 3,188,317 (June 8, 1965); *Chem. Abstr.*, **63**, 9947 (1965).
- (240) Hickner, R. A., U. S. Patent 3,190,885 (June 22, 1965); *Chem. Abstr.*, **63**, 9946 (1965).

- (241) Hickner, R. A., Bakke, W. W., and Judd, C. I., U. S. Patent 3,072,652 (Jan 8, 1963); *Chem. Abstr.*, **58**, 12569 (1963).
- (242) Hickner, R. A., and Judd, C. I., U. S. Patent 3,072,672 (Jan 8, 1963); *Chem. Abstr.*, **58**, 12568 (1963).
- (243) Hillers, S., *Vopr. Ispol'z. Pentozansoderzh. Syr'ya, Tr. Vses. Soveshch., Riga, 1955*, 451 (1958); *Chem. Abstr.*, **53**, 16388 (1959).
- (244) Hillers, S., Egerts, V., and Simanska, M., *Furazolidon, Akad. Nauk Latv. SSR, Inst. Organ. Sinteza*, **17** (1962); *Chem. Abstr.*, **59**, 3719 (1963).
- (245) Hillers, S., Egerts, V., Simanska, M., and Germane, S., *Latvijas PSR Zinatnu Akad. Vestis, Kim. Ser.*, **4**, 577 (1962); *Chem. Abstr.*, **59**, 8127 (1963).
- (246) Hillers, S., and Kalnbergs, *Furazolidon, Akad. Nauk Latv. SSR, Inst. Organ. Sinteza*, **5** (1962); *Chem. Abstr.*, **59**, 10015 (1963).
- (247) Hillers, S., and Kalnbergs, R., USSR Patent 160,508 (Jan 31, 1964); *Chem. Abstr.*, **60**, 14510 (1964).
- (248) Hodgins, T. S., and Hovey, A. G., British Patent 642,453 (Sept 6, 1950); *Chem. Abstr.*, **46**, 133 (1952).
- (249) Holstead, C., and Lamberton, A. H., *J. Chem. Soc.*, 1886 (1952).
- (250) Homeyer, A. H., U. S. Patent 2,399,118 (April 23, 1946); *Chem. Abstr.*, **40**, 4084 (1946). Divisions: U. S. Patents 2,437,388, 2,437,389, and 2,437,390; *Chem. Abstr.*, **42**, 4613 (1948).
- (251) Horn, R. C., Moffett, S. M., and Craig, L. E., U. S. Patent 3,133,932 (May 19, 1964); *Chem. Abstr.*, **61**, 7020 (1964).
- (252) Horton-Smith, C., and Long, P. L., *Ann. Trop. Med. Parasitol.*, **51**, 117 (1957); *Chem. Abstr.*, **51**, 12209 (1957).
- (253) Hoshiai, T., Akao, S., Tamura, S., Ishibashi, Y., and Yamaoka, K., *Nippon Saikigaku Zasshi*, **17**, 196 (1962); *Chem. Abstr.*, **60**, 13608 (1964).
- (254) Hsu, Chiao-Mu, *J. Taiwan Pharm. Assoc.*, **12**, 81 (1960); *Chem. Abstr.*, **55**, 24932 (1961).
- (255) Hyne, J. B., *J. Am. Chem. Soc.*, **81**, 6058 (1959).
- (256) Hyne, J. B., and Calosing, R., *Chem. Ind. (London)*, 488 (1963).
- (257) Ide, W. S., and Baltzly, R., *J. Am. Chem. Soc.*, **70**, 1084 (1948).
- (258) Ingleby, R. F. J., British Patent 887,595 (Jan 17, 1962); *Chem. Abstr.*, **56**, 12904 (1962).
- (259) Ingleby, R. F. J., British Patent 893,689 (April 11, 1962); *Chem. Abstr.*, **57**, 12497 (1962).
- (260) Irikura, T., Masuzawa, K., Tada, M., and Uchida, H., *Yakugaku Zasshi*, **83**, 1175 (1963); *Chem. Abstr.*, **60**, 10664 (1964).
- (261) Ishimaru, T., *Nippon Kagaku Zasshi*, **81**, 1428 (1960); *Chem. Abstr.*, **56**, 3469 (1952).
- (262) Ishimaru, T., *Nippon Kagaku Zasshi*, **81**, 1589 (1960); *Chem. Abstr.*, **56**, 3470 (1962).
- (263) Iwakura, Y., and Izawa, S., *J. Org. Chem.*, **29**, 379 (1964).
- (264) Iwakura, Y., and Izawa, S., Japanese Patent 1590 (Jan 28, 1965); *Chem. Abstr.*, **62**, 14684 (1965).
- (265) Iwakura, Y., and Taneda, Y., *J. Am. Chem. Soc.*, **24**, 1992 (1959).
- (266) Izrailet, L. I., *Materialy 1-go (Pervogo) Soveshch. po Aktual'n Vopr. Klinich. Biokhim., Riga, Sb*, 119 (1962); *Chem. Abstr.*, **59**, 14484 (1963).
- (267) Jackson, D., and Robson, J. M., *J. Endocrinol.*, **15**, 355 (1957); *Chem. Abstr.*, **51**, 18309 (1957).
- (268) Janeczek, V., Czech Patent 113,096 (Dec 15, 1964); *Chem. Abstr.*, **63**, 17048 (1965).
- (269) Jefferson Chemical Co., British Patent 883,994 (Dec 6, 1961); *Chem. Abstr.*, **58**, 2454 (1963).
- (270) Jeffries, S. F., U. S. Patent 3,149,041 (Sept 15, 1964); *Chem. Abstr.*, **61**, 13137 (1964).
- (271) Jeney, E., and Zsolnai, T., *Zentr. Bakteriolog., Parasitenk., Abt. I, Org.*, **189**, 454 (1963); *Chem. Abstr.*, **61**, 8655 (1964).
- (272) Jensen, K. A., *Dansk. Tid. Farm.*, **16**, 1 (1942); *Chem. Abstr.*, **37**, 4375 (1943).
- (273) Jensen, L. S., Saxena, H. C., and McGinnis, J., *Poultry Sci.*, **40**, 1524 (1961); *Chem. Abstr.*, **56**, 9198 (1962).
- (274) Jibiki, Y., Japanese Patent 26,680 (Dec 23, 1963); *Chem. Abstr.*, **60**, 6850 (1964).
- (275) Johnston, R. G., and Kidd, D., *J. Chem. Soc.*, 4730 (1964).
- (276) Johnson, T. B., and Guest, H. H., *Am. Chem. J.*, **44**, 453 (1911); *Chem. Abstr.*, **5**, 286 (1911).
- (277) Johnson, T. B., and Langley, R. W., *Am. Chem. J.*, **44**, 352 (1911); *Chem. Abstr.*, **5**, 84 (1911).
- (278) Jones, J. I., *Chem. Ind. (London)* 1454 (1956).
- (279) Jones, J. I., *J. Chem. Soc.*, 2735 (1957).
- (280) Jucker, E., Lindenmann, A., Schenker, E., Flueckiger, E., and Taeschler, M., *Arzneimittel-Forsch.*, **13**, 269 (1963); *Chem. Abstr.*, **61**, 1786 (1964).
- (281) Juskiewicz, T., and Zorawski, C., *Med. Weterynar.*, **14**, 280 (1958); *Chem. Abstr.*, **53**, 2366 (1959).
- (282) Kaminsky, D., Dubnick, B., and Anderson, F. E., *J. Med. Chem.*, **7**, 367 (1964); *Chem. Abstr.*, **61**, 3098 (1964).
- (283) Kaneko, T., and Inui, T., *Nippon Kagaku Zasshi*, **82**, 1075 (1961); *Chem. Abstr.*, **59**, 590 (1963).
- (284) Kaneko, T., and Inui, T., *Bull. Chem. Soc. Japan*, **35**, 1145 (1962); *Chem. Abstr.*, **57**, 9944 (1962).
- (285) Kaneko, T., Okuda, N., and Uono, H., Japanese Patent 24,457 (Oct 31, 1964); *Chem. Abstr.*, **62**, 11818 (1965).
- (286) Katchalski, E., and Ben-Ishai, D., *J. Org. Chem.*, **15**, 1067 (1950).
- (287) Kefauver, D. F., and Drupa, I., *Antibiot. Chemotherapy*, **10**, 688 (1960); *Chem. Abstr.*, **55**, 12534 (1961).
- (288) Kefauver, D. F., Paberz, I., and McNamara, T. F., *Antibiot. Ann., 1958-1959*, 81 (1959); *Chem. Abstr.*, **54**, 12385 (1960).
- (289) Kelly, W. D., Roth, P. H., and Taylor, L. D., Belgian Patent 619,075 (Dec 18, 1962); *Chem. Abstr.*, **58**, 9788 (1963).
- (290) Knorr, L., and Rössler, P., *Ber.*, **36**, 1278 (1903).
- (291) Koebner, A., and Senogles, E., British Patent 980,393 (Jan 13, 1965); *Chem. Abstr.*, **62**, 7570 (1965).
- (292) Kondo, M., Hayashi, M., and Mizuno, D., *Yakugaku Zasshi*, **83**, 386 (1963); *Chem. Abstr.*, **59**, 4361 (1963).
- (293) Koschucharov, P., and Harisanova, T., *Pharmazie*, **15**, 492 (1960); *Chem. Abstr.*, **56**, 11712 (1962).
- (294) Kovalenko, A. D., *Tr. Ukr. Nauchn. Konf. po Probl. Kishchn. Infektsii, Kiev*, 227 (1961); *Chem. Abstr.*, **60**, 13610 (1964).
- (295) Kreher, R., and Bockhorn, G. H., *Angew. Chem.*, **76**, 681 (1964).
- (296) Kreher, R., and Kuehling, D., *Angew. Chem.*, **77**, 42 (1965).
- (297) Kulkarni, S. R., and Zimmerman, H. K., Jr., *Ann.*, **684**, 223 (1965).
- (298) Kuoriyasu, C., and Watanabe, S., *Nippon Juigaku Zasshi*, **25**, 337 (1963); *Chem. Abstr.*, **60**, 14892 (1964).
- (299) Kutner, A., *J. Org. Chem.*, **26**, 3495 (1961).
- (300) Laboratories O M Société, Anon., British Patent 838,759 (June 22, 1960); *Chem. Abstr.*, **55**, 2688 (1961).
- (301) Laboratories O M Société, Anon., French Patent M1970 (Sept 16, 1963); *Chem. Abstr.*, **60**, 2937 (1964).
- (302) Laboratories del Dr. Esteve, S. A., Spanish Patent 296,313 (March 4, 1964); *Chem. Abstr.*, **61**, 14479 (1964).

- (303) LeDouarec, J. C., Regner, G., Canevari, R., French Patent M 1421 (Aug 27, 1962); *Chem. Abstr.*, **60**, 1759 (1964).
- (304) Lee, C. M., and Kumler, W. D., *J. Am. Chem. Soc.*, **83**, 4596 (1961).
- (305) Leshner, G. Y., *Dissertation Abstr.*, **17**, 36 (1957).
- (306) Leshner, G. Y., and Surrey, A. R., *J. Am. Chem. Soc.*, **77**, 636 (1955).
- (307) Levin Chemicals, Ltd., and Krawczak, Z., French Patent 1,351,517 (Feb 7, 1964); *Chem. Abstr.*, **61**, 663 (1964).
- (308) Lewis, P. A., Miller, M. T., Berg, C. F., and Stone, L. R., *J. Assoc. Offic. Agr. Chemists*, **43**, 305 (1960); *Chem. Abstr.*, **54**, 18827 (1960).
- (309) Little, E. D., U. S. Patent 3,064,004 (Nov 13, 1962); *Chem. Abstr.*, **58**, 10208 (1963).
- (310) Little, E. D., and Pickens, D., U. S. Patent 3,157,668 (Nov 17, 1964); *Chem. Abstr.*, **62**, 4032 (1965).
- (311) Little, E. D., and Poon, B. T., U. S. Patent 3,108,115 (Oct 22, 1963); *Chem. Abstr.*, **60**, 2936 (1964).
- (312) Llusá, R. P., Spanish Patent 255,784 (Feb 11, 1960); *Chem. Abstr.*, **56**, 1457 (1962).
- (313) Lucas, F. R., *Poultry Sci.*, **34**, 440 (1955); *Chem. Abstr.*, **49**, 14170 (1955).
- (314) Ludwig, B. J., West, W. A., and Farnsworth, D. W., *J. Am. Chem. Soc.*, **76**, 2891 (1954).
- (315) Luhman, C. A., *J. Assoc. Agr. Chemists*, **40**, 463 (1957); *Chem. Abstr.*, **51**, 9033 (1957).
- (316) Luhman, C. A., *J. Assoc. Agr. Chemists*, **41**, 333 (1958); *Chem. Abstr.*, **52**, 15780 (1958).
- (317) Luhman, C. A., *J. Assoc. Agr. Chemists*, **43**, 310 (1960); *Chem. Abstr.*, **54**, 18827 (1960).
- (318) Lunsford, C. D., U. S. Patent 2,895,960 (July 21, 1959); *Chem. Abstr.*, **54**, 4619 (1960).
- (319) Lunsford, C. D., British Patent 893,252 (April 4, 1962); *Chem. Abstr.*, **57**, 16622 (1962).
- (320) Lunsford, C. D., U. S. Patent 3,062,826 (Nov 6, 1962); *Chem. Abstr.*, **58**, 9082 (1963).
- (321) Lunsford, C. D., U. S. Patent 3,062,828 (Nov 6, 1962); *Chem. Abstr.*, **58**, 10207 (1963).
- (322) Lunsford, C. D., German Patent 1,152,417 (Aug 8, 1963); *Chem. Abstr.*, **60**, 527 (1964).
- (323) Lunsford, C. D., German Patent 1,157,627 (Nov 26, 1963); *Chem. Abstr.*, **60**, 9281 (1964).
- (324) Lunsford, C. D., German Patent 1,198,368 (Aug 12, 1965); *Chem. Abstr.*, **63**, 14867 (1965).
- (325) Lunsford, C. D., Mays, R. P., and Murphey, R. S., *J. Am. Chem. Soc.*, **82**, 1166 (1960).
- (326) Lynn, J. W., U. S. Patent 2,975,187 (March 14, 1961); *Chem. Abstr.*, **55**, 16568 (1961).
- (327) Marciszewski, H., *Dissertationes Pharm.*, **11**, 321 (1959); *Chem. Abstr.*, **54**, 13556 (1960).
- (328) Markley, F. X., Horton, R. L., and Weinberger, K. A., French Patent Addn. 80,105 (March 22, 1963); addn. to French Patent 1,284,520; *Chem. Abstr.*, **59**, 10058 (1963).
- (329) Marton, J., Szarvas, T., Tanacs, B., and Teplan, I., *Chem. Ind. (London)*, 1427 (1962).
- (330) Matsui, M., Araki, T., and Oka, Y., *Takeda Kenkyusho Nempo*, **21**, 72 (1962); *Chem. Abstr.*, **60**, 2076 (1964).
- (331) Matveev, I. S., *Zh. Obshch. Khim.*, **34**, 3417 (1964); *Chem. Abstr.*, **62**, 4019 (1965).
- (332) Matveev, I. S., and Politan, N. N., *Khim. Geterotskii Soedin. Akad. Nauk. Latv. SSR*, 467 (1965); *Chem. Abstr.*, **63**, 13234 (1965).
- (333) Maxwell, D. R., and Wragg, W. R., British Patent 943,739 (Dec 4, 1963); *Chem. Abstr.*, **60**, 5521 (1964).
- (334) May and Baker Ltd., Belgian Patent 620,235 (Jan 14, 1963); *Chem. Abstr.*, **59**, 7541 (1963).
- (335) May and Baker Ltd., Belgian Patent 620,236 (Jan 14, 1963); *Chem. Abstr.*, **59**, 6418 (1963).
- (336) McCabe, W. R., Davis, J. C., Anderson, B. R., and Jackson, G. G., *New Engl. J. Med.*, **263**, 927 (1960); *Chem. Abstr.*, **56**, 2849 (1962).
- (337) McCabe, W. R., Jackson, G. G., and Kozij, V. M., *Antibiot. Ann., 1959-1960*, 776 (1960); *Chem. Abstr.*, **54**, 17722 (1960).
- (338) McCortney, M. G., and Naber, E. C., *Poultry Sci.*, **39**, 1361 (1960); *Chem. Abstr.*, **55**, 18906 (1961).
- (339) McDonald, B. E., Bird, H. R., and Strong, F. M., *Proc. Soc. Exptl. Biol. Med.*, **113**, 728 (1963); *Chem. Abstr.*, **60**, 2091 (1964).
- (340) McKay, A. F., *J. Org. Chem.*, **16**, 1395 (1951).
- (341) McKay, A. F., and Braun, R. O., *J. Org. Chem.*, **16**, 1829 (1951).
- (342) McKay, A. F., and Tarlton, E. J., *J. Am. Chem. Soc.*, **74**, 2978 (1952).
- (343) McLaughlin, D. K., and Chester, D. K., *Poultry Sci.*, **38**, 353 (1959); *Chem. Abstr.*, **53**, 19137 (1959).
- (344) Mecke, R., and Mecke, R., *Ber.*, **89**, 343 (1956).
- (345) Mecke, R., Mecke, R., and Lüttringhaus, A., *Ber.*, **90**, 975 (1957).
- (346) Michels, J. G., U. S. Patent 2,898,335 (Aug 4, 1959); *Chem. Abstr.*, **54**, 2356 (1960).
- (347) Michels, J. G., Gever, G., and Wei, P. H. L., *J. Med. Pharm. Chem.*, **5**, 1042 (1962); *Chem. Abstr.*, **58**, 5602 (1963).
- (348) Midland Silicones Ltd., British Patent 868,188 (May 17, 1961); *Chem. Abstr.*, **55**, 22905 (1961).
- (349) Milies, E., and Monti, M., *Acta Neurol. Latinoam.*, **8**, (1962); *Chem. Abstr.*, **61**, 16642 (1964).
- (350) Minyard, A., Ferrell, J., Guerra, F. J., and Pair, D. B., *Texas J. Pharm.*, **4**, 346 (1963); *Chem. Abstr.*, **60**, 6112 (1964).
- (351) Misiti, D., Amato, A., and Rosnati, V., *Gazz. Chim. Ital.*, **93**, 1118 (1963); *Chem. Abstr.*, **60**, 4122 (1964).
- (352) Miyake, A., Japanese Patent 18,589 (Dec 23, 1960); *Chem. Abstr.*, **55**, 21676 (1961).
- (353) Moersch, G. W., and Creger, P. L., *J. Heterocyclic Chem.*, **2**, 207 (1965).
- (354) Montale, P., Gay, A., and Damasio, E., *Arch. "E. Maragliano" Pathol. Clin.*, **18**, 825 (1962); *Chem. Abstr.*, **59**, 15637 (1963).
- (355) Montale, P., Peris, G., and Marchese, S., *Arch. "E. Maragliano" Pathol. Clin.*, **18**, 371 (1962); *Chem. Abstr.*, **57**, 14402 (1962).
- (356) Morrison, J. A., *Arch. Intern. Pharmacodyn.*, **157**, 385 (1965); *Chem. Abstr.*, **64**, 1189 (1966).
- (357) Mousseron, M., Winternitz, F., and Mousseron-Canet, M., *Compt. Rend.*, **235**, 373 (1952).
- (358) Mousseron, M., Winternitz, F., and Mousseron-Canet, M., *Bull. Soc. Chim. France*, 737 (1953).
- (359) Munoz, M. S., *Anales Real Acad. Farm.*, **28**, 181 (1962); *Chem. Abstr.*, **60**, 8564 (1964).
- (360) Murdock, S. A., U. S. Patent 3,075,947 (Jan 29, 1963); *Chem. Abstr.*, **58**, 10341 (1963).
- (361) Murdock, S. A., and Armen, A., U. S. Patent 3,026,295 (March 20, 1962); *Chem. Abstr.*, **57**, 6150 (1962).
- (362) Murdock, S. A., Davis, C. W., and Ehlers, F. A., U. S. Patent 3,072,599 (Jan 8, 1963); *Chem. Abstr.*, **58**, 14185 (1963).
- (363) Murdock, S. A., Davis, C. W., and Ehlers, F. A., U. S. Patent 3,083,179 (March 26, 1963); *Chem. Abstr.*, **58**, 14260 (1963).

- (364) Murdock, S. A., Davis, C. W., and Ehlers, F. A., U. S. Patent 3,084,138 (April 2, 1963); *Chem. Abstr.*, **59**, 1795 (1963).
- (365) Murdock, S. A., Traylor, T. G., and Lefferdink, T. B., U. S. Patent 3,026,287 (March 20, 1962); *Chem. Abstr.*, **57**, 3659 (1962).
- (366) Najer, H., Chabrier, P., and Delaby, R., *Bull. Soc. Chim. France*, 689 (1956).
- (367) Najer, H., Chabrier, P., and Giudicelli, R., *Compt. Rend.*, **238**, 690 (1954).
- (368) Najer, H., Chabrier, P., and Giudicelli, R., *Bull. Soc. Chim. France*, 1611 (1959).
- (369) Najer, H., Chabrier, P., Giudicelli, R., and Mabile, P., *Bull. Soc. Chim. France*, 471 (1957).
- (370) Najer, H., Chabrier, P., Giudicelli, R., and Mabile, P., *Bull. Soc. Chim. France*, 1069 (1957).
- (371) Najer, H., Chabrier, P., Giudicelli, R., Menin, J., and Duchemin, J., *Bull. Soc. Chim. France*, 1841 (1959).
- (372) Nakamura, N., and Sabino, I., *Takeda Kenkyusho Nempo*, **20**, 16 (1961); *Chem. Abstr.*, **58**, 743 (1963).
- (373) Nakanishi, M., and Oya, T., Japanese Patent 17,234 (Oct 23, 1962); *Chem. Abstr.*, **59**, 11499 (1963).
- (374) Nakanishi, M., and Oya, T., Japanese Patent 18,493 (Dec 4, 1962); *Chem. Abstr.*, **59**, 11512 (1963).
- (375) Nakazaki, M., and Arakawa, H., *Bull. Chem. Soc. Japan*, **34**, 453 (1961); *Chem. Abstr.*, **55**, 19886 (1961).
- (376) Nakazaki, M., and Arakawa, H., *Bull. Chem. Soc. Japan*, **34**, 1246 (1961); *Chem. Abstr.*, **57**, 2201 (1962).
- (377) Naneko, T., Okuda, N., and Uono, H., Japanese Patent 24,457 (Oct 31, 1964); *Chem. Abstr.*, **62**, 11818 (1965).
- (378) Nazarov, S., *Latvijas PSR Zinatnu Akad. Vestis*, 71 (1961); *Chem. Abstr.*, **56**, 9248 (1962).
- (379) Nemirowsky, *J. Prakt. Chem.*, [2] **31**, 175 (1885).
- (380) Newcomer, J. S., Smith, K. J., and Linder, J., U. S. Patent 2,860,166 (Nov 11, 1958); *Chem. Abstr.*, **53**, 9147 (1959).
- (381) Newman, M. S., *J. Am. Chem. Soc.*, **71**, 378 (1949).
- (382) Newman, M. S., and Edwards, W. M., *J. Am. Chem. Soc.*, **76**, 1840 (1954).
- (383) Newman, M. S., and Kutner, A., *J. Am. Chem. Soc.*, **73**, 4199 (1951).
- (384) Newman, M. S., and Weinberg, A. E., *J. Am. Chem. Soc.*, **78**, 4654 (1956).
- (385) Newman, M. S., and Weinberg, A. E., *J. Am. Chem. Soc.*, **79**, 2814 (1957).
- (386) Nicolaus, B. I. R., Mariani, L., Gallo, G., and Testa, E., *J. Org. Chem.*, **26**, 2253 (1961).
- (387) Norton, C. J., and Moss, T. E., U. S. Patent, 3,120,487 (Feb 4, 1964); *Chem. Abstr.*, **60**, 10450 (1964).
- (388) Norwich Pharmacal Co., British Patent 735,136 (Aug 17, 1955); *Chem. Abstr.*, **50**, 7874 (1956).
- (389) Norwich Pharmacal Co., British Patent 735,169 (Aug 17, 1955); *Chem. Abstr.*, **50**, 7875 (1956).
- (390) Norwich Pharmacal Co., French Patent CAM 33 (July 15, 1963); *Chem. Abstr.*, **59**, 15128 (1963).
- (391) N. V. Chemische Industrie Ranstad, Belgian Patent 620,332 (Nov 14, 1962); *Chem. Abstr.*, **59**, 5172 (1963).
- (392) N. V. Fabriek van Chemische Production, Belgian Patent 612,000 (Jan 15, 1962); *Chem. Abstr.*, **57**, 16880 (1962).
- (393) Oda, R., and Hata, M., *Nippon Kagaku Zasshi*, **82**, 1426 (1961); *Chem. Abstr.*, **58**, 3337 (1963).
- (394) Oda, R., and Isoda, K., Japanese Patent 17,595 (Nov 30, 1960); *Chem. Abstr.*, **55**, 20510 (1961).
- (395) Oda, R., Miyanoki, M., and Okano, M., *Bull. Chem. Soc. Japan*, **35**, 1309 (1962); *Chem. Abstr.*, **57**, 13748 (1962).
- (396) Oda, R., Miyanoki, M., and Okano, M., *Bull. Chem. Soc. Japan*, **35**, 1910 (1962); *Chem. Abstr.*, **59**, 3909 (1963).
- (397) Oda, R., Miyanoki, M., and Okano, M., *Bull. Chem. Soc. Japan*, **35**, 1915 (1962); *Chem. Abstr.*, **59**, 3909 (1963).
- (398) Oken, A., U. S. Patent 2,977,370 (March 28, 1961); *Chem. Abstr.*, **55**, 17652 (1961).
- (399) Olaj, O., and Maeder, A., Swiss Patent 372,027 (Nov 15, 1963); *Chem. Abstr.*, **60**, 12169 (1964).
- (400) Olesiuk, O. M., Roekel, H., and Beninato, L. P., *Poultry Sci.*, **36**, 383 (1957); *Chem. Abstr.*, **51**, 14975 (1957).
- (401) Olson, K. J., Dupree, R. W., Plomer, A., and Rowe, V. K., *J. Soc. Cosmetic Chemists*, **13**, 469 (1962); *Chem. Abstr.*, **58**, 10649 (1963).
- (402) Orgahell, N. V., Dutch Patent 97,978 (May 15, 1961); *Chem. Abstr.*, **58**, 11367 (1963).
- (403) Orphahell N. V., British Patent 949,315 (Feb 12, 1964); *Chem. Abstr.*, **60**, 10686 (1964).
- (404) Otto, *J. Prakt. Chem.*, [2] **44**, 17 (1891).
- (405) Owens, R. G., and Novotny, H. M., *Contrib. Boyce Thompson Inst.*, **20**, 151 (1959); *Chem. Abstr.*, **53**, 20666 (1959).
- (406) Paquin, A. M., *Z. Naturforsch.*, **1**, 518 (1946); *Chem. Abstr.*, **42**, 123 (1948).
- (407) Paterno, E., and Cingolani, E., *Gazz. Chim. Ital.*, **38**, 243 (1908); *Chem. Abstr.*, **2**, 1689 (1908).
- (408) Paul, M. F., Bender, R. C., and Humphrey, D., *Antibiot. Chemotherapy*, **11**, 345 (1961); *Chem. Abstr.*, **55**, 26156 (1961).
- (409) Paul, H. E., Ells, V. R., Kopko, F., and Bender, R. C., *J. Med. Pharm. Chem.*, **2**, 563 (1960); *Chem. Abstr.*, **55**, 7676 (1961).
- (410) Paul, M. F., Paul, H. E., Bender, R. C., Kopko, F., Harrington, C. M., Ells, V. R., and Buzard, J. A., *Antibiot. Chemotherapy*, **10**, 287 (1960); *Chem. Abstr.*, **54**, 21485 (1960).
- (411) Paul, H. E., Paul, M. F., Kopko, F., Bender, R. C., and Everett, G., *Endocrinology*, **53**, 585 (1953); *Chem. Abstr.*, **48**, 13961 (1954).
- (412) Pellon, J. J., U. S. Patent 2,954,366 (Sept 27, 1960); *Chem. Abstr.*, **55**, 4043 (1961).
- (413) Peppel, W. J., and Watkins, J. D., U. S. Patent 3,019,231 (Jan 30, 1962); *Chem. Abstr.*, **56**, 12748 (1962).
- (414) Perkow, W., *Arzneimittel-Forsch.*, **10**, 284 (1960); *Chem. Abstr.*, **54**, 16654 (1960).
- (415) Pesez, M., and Bartos, J., *Bull. Soc. Chim. France*, 1122 (1963).
- (416) Petkov, S., and Petkovova, R., *Sb. Cesk. Akad. Zemedel. Ved., Zivocisna Vyroba*, **6**, 69 (1961); *Chem. Abstr.*, **55**, 10619 (1961).
- (417) Petrow, V., Stephenson, O., and Wild, A. M., *J. Pharm. Pharmacol.*, **12**, 37 (1960); *Chem. Abstr.*, **54**, 16457 (1960).
- (418) Pfizer and Co., Inc., British Patent 865,796 (April 19, 1961); *Chem. Abstr.*, **55**, 22340 (1961).
- (419) Pichat, L., and Audinot, M., *Bull. Soc. Chim. France*, 2255 (1961).
- (420) Pierce, J. S., *J. Am. Chem. Soc.*, **50**, 241 (1928).
- (421) Pinchas, S., and Ben-Ishai, D., *Bull. Res. Council Israel*, **A6**, 166 (1957); *Chem. Abstr.*, **51**, 17455 (1957).
- (422) Pinchas, S., and Ben-Ishai, D., *J. Am. Chem. Soc.*, **79**, 4099 (1957).
- (423) Polichimica SAP Farmaceutici, S.p.t., Belgian Patent 635,608 (Nov 18, 1963); *Chem. Abstr.*, **61**, 16069 (1964).
- (424) Pomot, J. L., Belgian Patent 633,841 (Nov 4, 1963); *Chem. Abstr.*, **60**, 14509 (1964).
- (425) Pomot, J. L., French Patent 1,346,269 (Dec 20, 1963); *Chem. Abstr.*, **60**, 12017 (1964).
- (426) Poos, G. I., Carson, J. R., Rosenau, J. D., Roszkowski, A. P., Kelley, N. M., and McGowin, J., *J. Med. Chem.*, **6**, 266 (1963); *Chem. Abstr.*, **59**, 1610 (1963).

- (427) Pope, C. W., and Schaible, P. J., *Mich. State Univ., Agr. Expt. Sta. Quart. Bull.*, **40**, 857 (1958); *Chem. Abstr.*, **52**, 17444 (1958).
- (428) Post, G., *Progr. Fish Culturist*, **21**, 30 (1959); *Chem. Abstr.*, **53**, 20585 (1959).
- (429) Post, G., *Progr. Fish Culturist*, **24**, 182 (1962); *Chem. Abstr.*, **58**, 14495 (1963).
- (430) Post, G., and Keiss, R. E., *Progr. Fish Culturist*, **24**, 16 (1962); *Chem. Abstr.*, **56**, 10729 (1962).
- (431) Puttner, R., and Hafner, K., *Tetrahedron Letters*, 3119 (1964).
- (432) Rechka, J., and Kalous, J., *Sb. Vysoke Skoly Zemedel. Brne, Rada A*, 21(1961); *Chem. Abstr.*, **56**, 14700 (1962).
- (433) Redman, C. E., and Smyth, J. R., Jr., *Poultry Sci.*, **36**, 437 (1957); *Chem. Abstr.*, **51**, 15772 (1957).
- (434) Regnier, G., Canevari, R., and LeDouarec, J.-C., French Patent 1,395,085 (April 9, 1965); *Chem. Abstr.*, **64**, 2089 (1966).
- (435) Rich, A. G., *Dissertation Abstr.*, **22**, 4329 (1962); *Chem. Abstr.*, **57**, 9961 (1962).
- (436) Rivera-Anaya, J. D., and Berrocal, C. M., *J. Agr. Univ. Puerto Rico*, **47**, 180 (1963); *Chem. Abstr.*, **60**, 2222 (1964).
- (437) Robbins Co., Inc., A. H., British Patent 888,594 (Jan 31, 1962); *Chem. Abstr.*, **57**, 2227 (1962).
- (438) Roberts, C. W., and Haigh, D. H., U. S. Patent 3,162,645 (Dec 22, 1964); *Chem. Abstr.*, **62**, 7763 (1965).
- (439) Rodzewich, E. A., Belgian Patent 630,412 (Aug 1, 1963); *Chem. Abstr.*, **61**, 6704 (1964).
- (440) Rosenberg, D. W., Woodward, R. D., and Kline, A. E., *J. Am. Vet. Med. Assoc.*, **141**, 958 (1962); *Chem. Abstr.*, **58**, 4943 (1963).
- (441) Rosnati, V., and Misiti, D., *Rend. Ist. Super. Sanita*, **23**, 610 (1960); *Chem. Abstr.*, **55**, 5464 (1961).
- (442) Rosnati, V., and Misiti, D., *Tetrahedron*, **9**, 175 (1960).
- (443) Roviralta, C. C., Spanish Patent 276,359 (May 23, 1962); *Chem. Abstr.*, **60**, 530 (1964).
- (444) Roviralta, C. C., and Coll, A. L. P., Spanish Patent 281,691 (Oct 31, 1962); *Chem. Abstr.*, **60**, 2938 (1964).
- (445) Roy, D. N., Lipton, S. H., Bird, H. R., and Strong, F. M., *Poultry Sci.*, **40**, 55 (1961); *Chem. Abstr.*, **55**, 18998 (1961).
- (446) Rylander, P. N., Jr., and Junk, W. A., Jr., U. S. Patent 2,840,511 (June 24, 1958); *Chem. Abstr.*, **52**, 16735 (1958).
- (447) Ryley, J. F., and Stacey, G. J., *Parasitology*, **53**, 303 (1963); *Chem. Abstr.*, **59**, 11935 (1963).
- (448) Saito, T., *Bull. Chem. Soc. Japan*, **37**, 624 (1964); *Chem. Abstr.*, **63**, 5755 (1964).
- (449) Salmon, W. D., and Newberne, P. M., *J. Nutr.*, **76**, 483 (1962); *Chem. Abstr.*, **59**, 15806 (1963).
- (450) Samuels, R., and Stouder, D. J., *J. Protozool.*, **9**, 249 (1962); *Chem. Abstr.*, **58**, 4836 (1963).
- (451) Sanders, H. J., Edmunds, R. T., and Stillman, W. B., *Ind. Eng. Chem.*, **47**, 358 (1955); *Chem. Abstr.*, **49**, 8560 (1955).
- (452) Sandler, S. R., Berg, F., and Kitazawa, G., *J. Appl. Polymer Sci.*, **9**, 1994 (1965).
- (453) Sandoz, Ltd., Belgian Patent 610,039 (May 7, 1962); *Chem. Abstr.*, **58**, 1469 (1963).
- (454) Sato, S., Yoshida, I., and Kuwahara, S., *Japan. J. Microbiol.*, **4**, 419 (1960); *Chem. Abstr.*, **56**, 5211 (1962).
- (455) Sayigh, A. A., and Ulrich, H., *J. Chem. Soc.*, 3148 (1961).
- (456) Schefczik, E., and Pasedach, H., German Patent 1,134,381 (Aug 9, 1962); *Chem. Abstr.*, **58**, 1464 (1963).
- (457) Schefczik, E., and Pasedach, H., German Patent 1,158,075 (Aug 28, 1963); *Chem. Abstr.*, **60**, 6850 (1965).
- (458) Schefczik, E., and Pasedach, H., German Patent 1,162,372 (Feb 6, 1964); *Chem. Abstr.*, **60**, 12016 (1964).
- (459) Scheibler, H., and Scheibler, U., *Ber.*, **87**, 379 (1954).
- (460) Scheurlen, H., and Schmidt, K. L., German Patent 1,109,876 (Appl. July 2, 1956); *Chem. Abstr.*, **56**, 1619 (1962).
- (461) Schipper, E., Chinery, E., and Nichols, J., *J. Org. Chem.*, **26**, 4145 (1961).
- (462) Schnabel, E., *Ann.*, **659**, 168 (1962).
- (463) Schnabel, E., *Peptides, Proc. European Symp., 5th Oxford, 1962*, 77 (1963); *Chem. Abstr.*, **61**, 16145 (1964).
- (464) Scholtissek, C., *Ber.*, **89**, 2562 (1956).
- (465) Schöpf, C., and Wüst, W., *Ann.*, **626**, 150 (1959).
- (466) Schuler, M., Helfenberger, H., and Lutz, K., French Patent 1,339,156 (Oct 4, 1963); *Chem. Abstr.*, **60**, 4154 (1964).
- (467) Schuller, W. H., and Kerle, E. J., U. S. Patent 2,786,043 (March 19, 1957); *Chem. Abstr.*, **51**, 11758 (1957).
- (468) Scotti, F., and Frazza, E. J., U. S. Patent 3,138,606 (June 23, 1964); *Chem. Abstr.*, **61**, 7023 (1964).
- (469) Scuri, R., and Failla, L., *Farmaco (Pavia), Ed. Sci.*, **19**, 301 (1964); *Chem. Abstr.*, **61**, 9919 (1964).
- (470) Sergeev, P. G., and Ivanov, S. N., *J. Gen. Chem. USSR*, **7**, 1495 (1937); *Chem. Abstr.*, **32**, 2534 (1938).
- (471) Shachat, N., and Bagnell, J. J., Jr., *J. Org. Chem.*, **28**, 991 (1963).
- (472) Shapiro, D., *J. Org. Chem.*, **15**, 1027 (1950).
- (473) Shelton, D. C., and Olson, N. O., *Poultry Sci.*, **38**, 575 (1959); *Chem. Abstr.*, **53**, 19138a (1959).
- (474) Shelton, D. C., Olson, N. O., and Weakley, C. E., *Poultry Sci.*, **37**, 610 (1958); *Chem. Abstr.*, 2456 (1959).
- (475) Siegmann, O., *Zentr. Veterinaarmed.*, **7**, 94 (1960); *Chem. Abstr.*, **54**, 8975 (1960).
- (476) Signaigo, F. K., U. S. Patent 2,459,547 (Jan 18, 1949); *Chem. Abstr.*, **43**, 3196 (1949).
- (477) Sisido, K., Hukuoka, K., Tuda, M., and Nozaki, H., *J. Org. Chem.*, **27**, 2663 (1962).
- (478) Skulski, M., Garmaise, D. L., and McKay, A. F., *Can. J. Chem.*, **34**, 815 (1956).
- (479) Smith, D. A., *Nature*, **197**, 285 (1963).
- (480) Smith, J. L., and Harrington, R. C., Jr., U. S. Patent 2,891,962 (June 23, 1959); *Chem. Abstr.*, **54**, 1546 (1960).
- (481) Smolik, S., Novacek, A., and Kopecky, J., Czech Patent 105,032 (Sept 15, 1962); *Chem. Abstr.*, **60**, 8036 (1964).
- (482) Smolinsky, G., and Feuer, B. I., *J. Am. Chem. Soc.*, **86**, 3085 (1964).
- (483) Smyth, J. R., Jr., Anderson, D. L., and Fox, T. W., *Poultry Sci.*, **38**, 288 (1959); *Chem. Abstr.*, **53**, 19061 (1959).
- (484) Société anon. des manufactures des glaces et produits chimiques de Saint-Gobain, Chauny et Cirey, British Patent 720,586 (Dec 22, 1954); *Chem. Abstr.*, **50**, 1922 (1956).
- (485) Société anon. des manufactures des glaces et produits chimiques de Saint-Gobain, Chauny et Cirey, British Patent 834,563 (May 11, 1960); *Chem. Abstr.*, **54**, 20321 (1960).
- (486) Sönnerskog, S., *Acta Chem. Scand.*, **10**, 467 (1956); *Chem. Abstr.*, **51**, 3180 (1957).
- (487) Sovish, R. C., U. S. Patent 3,119,833 (Jan 28, 1964); *Chem. Abstr.*, **60**, 10686 (1964).
- (488) Spears, A. W., III, Routh, W. E. Lassiter, C. W., and Bell, J. H., Belgian Patent 631,043 (Aug 1, 1963); *Chem. Abstr.*, **61**, 14891 (1964).
- (489) Spence, T. C., and Murdock, S. A., U. S. Patent 2,935,426 (May 3, 1960); *Chem. Abstr.*, **54**, 20232 (1960).
- (490) Spencer, C. F., German Patent 1,171,434 (June 4, 1964); *Chem. Abstr.*, **61**, 5656 (1964).

- (491) Speranza, G. P., and Peppel, W. J., *J. Org. Chem.*, **23**, 1922 (1958).
- (492) Sprinson, D. B., *J. Am. Chem. Soc.*, **63**, 2249 (1941).
- (493) Stabler, R. M., *J. Parasitol.*, **43**, 280 (1957); *Chem. Abstr.*, **51**, 14996 (1957).
- (494) Stahnecker, E., and Mueller-Tamm, H., German Patent 1,161,425 (Jan 16, 1964); *Chem. Abstr.*, **60**, 9442 (1964).
- (495) Steele, A. B., U. S. Patent 2,868,801 (Jan 13, 1959); *Chem. Abstr.*, **53**, 10261 (1959).
- (496) Steele, A. B., O'Neal, J. B., and Anderson, J. R., U. S. Patent 2,932,675 (April 12, 1960); *Chem. Abstr.*, **54**, 23307 (1960).
- (497) Steinemann, W., U. S. Patent 2,873,267 (Feb 10, 1959); *Chem. Abstr.*, **54**, 2757 (1960).
- (498) Steinemann, W., Swiss Patent 359,138 (Feb 15, 1962); *Chem. Abstr.*, **58**, 1464 (1963).
- (499) Sterling, G. B., and Zimmerman, R. L., U. S. Patent 3,092,605 (June 14, 1963); *Chem. Abstr.*, **59**, 5348 (1963).
- (500) Sternieri, E., Giaroli, M., and Bernardi, M., *Biochim. Biol. Sper.*, **2**, 426 (1963); *Chem. Abstr.*, **61**, 15213 (1964).
- (501) Steyermark, P. R., U. S. Patent 3,120,510 (Feb 4, 1964); *Chem. Abstr.*, **60**, 9349 (1964).
- (502) Stiles, P. G., *Poultry Sci.*, **41**, 1336 (1962); *Chem. Abstr.*, **58**, 7172 (1963).
- (503) Stoffel, P. J., and Dixon, W. D., *J. Org. Chem.*, **29**, 978 (1964).
- (504) Stoffel, P. J., and Speziale, A. J., *J. Org. Chem.*, **28**, 2814 (1963).
- (505) Stoll, A., and Petrazilka, T., *Helv. Chim. Acta*, **35**, 589 (1952).
- (506) Stone, I., U. S. Patent 3,089,818 (May 14, 1963); *Chem. Abstr.*, **59**, 3723 (1963).
- (507) Stone, L. R., *J. Assoc. Offic. Agr. Chemists*, **47**, 562 (1964); *Chem. Abstr.*, **61**, 8824 (1964).
- (508) Stone, L. R., *J. Assoc. Offic. Agr. Chemists*, **47**, 565 (1964); *Chem. Abstr.*, **61**, 6284 (1964).
- (509) Stone, R., Lewis, P. A., Miller, M. T., and Berg, C. F., *J. Assoc. Offic. Agr. Chemists*, **42**, 615 (1959); *Chem. Abstr.*, **53**, 18329 (1959).
- (510) Stradins, J., Aizpuriete, I., and Hillers, S., *Latvijas PSR Zinatnu Akad. Vestis, Kim. Ser.*, **29** (1963); *Chem. Abstr.*, **60**, 1975 (1964).
- (511) Stradins, J., Hillers, S., and Dzene, A., *Latvijas PSR Zinatnu Akad. Vestis*, **12**, 71 (1959); *Chem. Abstr.*, **54**, 20085 (1960).
- (512) Stradins, J., Hillers, S., and Liepina, L., *Latvijas PSR Zinatnu Akad. Vestis*, **1**, 113 (1958); *Chem. Abstr.*, **52**, 14287 (1958).
- (513) Stradins, J., Hillers, S., and Yurev, Y. K., *Dokl. Akad. Nauk SSSR*, **129**, 816 (1959); *Chem. Abstr.*, **54**, 6363 (1960).
- (514) Stratton, J. M., and Wilson, F. J., *J. Chem. Soc.*, 1133 (1932).
- (515) Stratton, J. M., and Wilson, F. J., *J. Roy. Tech. Coll. (Glasgow)*, **3**, 21 (1933); *Chem. Abstr.*, **27**, 3203 (1933).
- (516) Sudon, O., Swedish Patent 148,559 (Jan 25, 1955); *Chem. Abstr.*, **50**, 2679 (1956).
- (517) Sullivan, E. J., U. S. Patent 3,146,193 (Aug 25, 1964); *Chem. Abstr.*, **61**, 14364 (1964).
- (518) Surrey, A. R., U. S. Patent 2,843,585 (July 15, 1958); *Chem. Abstr.*, **53**, 2255 (1959).
- (519) Svedres, E. V., U. S. Patent 3,132,074 (May 5, 1964); *Chem. Abstr.*, **61**, 6875 (1964).
- (520) Swintosky, J. V., U. S. Patent 3,131,197 (April 28, 1964); *Chem. Abstr.*, **61**, 3114 (1964).
- (521) Swirska, A., *Przemysl. Chem.*, **40**, 590 (1961); *Chem. Abstr.*, **57**, 11177 (1962).
- (522) Swirska, A., *Acta Polon. Pharm.*, **19**, 317 (1962); *Chem. Abstr.*, **60**, 4137 (1964).
- (523) Swirska, A., and Lange, J., *Przemysl. Chem.*, **13**, 400 (1957); *Chem. Abstr.*, **52**, 3140 (1958).
- (524) Swirska, A., and Michalski, K., *Acta Polon. Pharm.*, **19**, 459 (1962); *Chem. Abstr.*, **60**, 13234 (1964).
- (525) Synowiedzki, Z., Polish Patent 46,318 (Dec 4, 1962); *Chem. Abstr.*, **60**, 378 (1964).
- (526) Tabushi, I., and Oda, R., *Nippon Kagaku Zasshi*, **84**, 162 (1963); *Chem. Abstr.*, **59**, 15131 (1963).
- (527) Tanaka, I., and Iwase, U., Japanese Patent 15,619 (Oct 1, 1962); *Chem. Abstr.*, **59**, 11499 (1963).
- (528) Tazawa, Y., Japanese Patent 18,694 (Sept 18, 1963); *Chem. Abstr.*, **60**, 2936 (1964).
- (529) Tazawa, Y., Japanese Patent 22,884 (Oct 28, 1963); *Chem. Abstr.*, **60**, 4152 (1964).
- (530) Teramura, K., *Mem. Fac. Ind. Arts, Kyoto Tech. Univ. Sci. Technol.*, **8**, 53 (1959); *Chem. Abstr.*, **55**, 562 (1961).
- (531) Teramura, K., and Oda, R., *Yuki Gosei Nagaku Kyokaishi*, **18**, 896 (1960); *Chem. Abstr.*, **55**, 5524 (1961).
- (532) Testard, J., French Patent 1,104,065 (Nov 16, 1955); *Chem. Abstr.*, **52**, 20198 (1958).
- (533) Testard, J. M. A., French Patent 1,104,082 (Nov 16, 1955); *Chem. Abstr.*, **53**, 6253 (1959).
- (534) Thomsen, A. L., *Ber.*, **11**, 2136 (1878).
- (535) Tousignant, W. F., U. S. Patent 3,152,141 (Oct 6, 1964); *Chem. Abstr.*, **62**, 564 (1965).
- (536) Tousignant, W. F., and Baker, A. W., *J. Org. Chem.*, **22**, 166 (1957).
- (537) Tousignant, W. F., and Walles, W. E., U. S. Patent 2,941,907 (June 21, 1960); *Chem. Abstr.*, **54**, 21668 (1960).
- (538) Tousignant, W. F., and Walles, W. E., U. S. Patent 3,004,950 (Oct 17, 1961); *Chem. Abstr.*, **56**, 14484 (1962).
- (539) Tousignant, W. F., and Walles, W. E., U. S. Patent 3,033,830 (May 8, 1962); *Chem. Abstr.*, **57**, 12495 (1962).
- (540) Tousignant, W. F., and Walles, W. E., U. S. Patent 3,124,494 (March 10, 1964); *Chem. Abstr.*, **60**, 13090 (1964).
- (541) Tousignant, W. F., and Walles, W. E., U. S. Patent 3,133,904 (May 19, 1964); *Chem. Abstr.*, **61**, 5808 (1964).
- (542) Tousignant, W. F., Walles, W. E., and Houtman, T., Jr., U. S. Patent 2,948,656 (Aug 9, 1960); *Chem. Abstr.*, **54**, 25608 (1960).
- (543) Trask, J. L., and Tousignant, W. F., U. S. Patent 2,826,587 (March 11, 1958); *Chem. Abstr.*, **52**, 11125 (1958).
- (544) Trieschmann, H. G., German Patent 917,972 (Sept 10, 1954); *Chem. Abstr.*, **52**, 11950 (1958).
- (545) Trieschmann, H. G., and Reuter, L., German Patent 883,902 (July 23, 1953); *Chem. Abstr.*, **52**, 11950 (1958).
- (546) Truhaut, R., and Deysson, G., *Ann. Pharm. Franc.*, **15**, 433 (1957); *Chem. Abstr.*, **52**, 6617 (1958).
- (547) Truhaut, R., and Deysson, G., *Compt. Rend.*, **244**, 2257 (1957).
- (548) Tsuzuki, R., Ichikawa, K., and Kase, M., *J. Org. Chem.*, **25**, 1009 (1960).
- (549) Tsuzuki, T., Ichikawa, K., and Kase, M., Japanese Patent 1261 (April 30, 1962); *Chem. Abstr.*, **58**, 10221 (1963).
- (550) Tsuzuki, T., Ichikawa, K., and Kase, M., Japanese Patent 18,190 (Nov 20, 1962); *Chem. Abstr.*, **59**, 11499 (1963).
- (551) Uenaka, H., Japanese Patent 20,295 (Oct 24, 1961); *Chem. Abstr.*, **59**, 11724 (1963).
- (552) Ueno, S., Japanese Patent 16,050 (Oct 8, 1962); *Chem. Abstr.*, **59**, 1031 (1963).
- (553) Uriach, J., and Pujol, R., *Galenica Acta*, **13**, 415 (1960); *Chem. Abstr.*, **55**, 19137 (1961).

- (554) Vander Noot, G., *J. Animal Sci.*, **17**, 313 (1958); *Chem. Abstr.*, **52**, 16648 (1958).
- (555) Van Dijk, C. P., and Murdock, S. A., U. S. Patent 3,106,482 (Oct 8, 1963); *Chem. Abstr.*, **60**, 3158 (1964).
- (556) Vanini, G. C., Mandras, A., Mannini, A., and Salvatore V., *Igiene Mod.* (Parma), **54**, 510 (1961); *Chem. Abstr.*, **57**, 5117 (1962).
- (557) Vanini, G. C., Mandras, A., Mannini, A., and Salvatore, V., *Giorn. Ital. Chemioterap.*, **5-9**, 55 (1962); *Chem. Abstr.*, **57**, 15607 (1962).
- (558) Vesterman, Sh. G., USSR Patent 158,577 (Nov 12, 1963); *Chem. Abstr.*, **60**, 10687 (1964).
- (559) Viard, M. J., British Patent 693,325 (June 24, 1953); *Chem. Abstr.*, **48**, 1417 (1954).
- (560) Viard, M. J., French Patent 1,099,905 (Sept 14, 1955); *Chem. Abstr.*, **52**, 20198 (1958).
- (561) Viard, M. J., U. S. Patent 2,773,067 (Dec 4, 1956); *Chem. Abstr.*, **51**, 3667 (1957).
- (562) Vieles, P., and Sequin, J., *Bull. Soc. Chim. France*, **287** (1953).
- (563) Vignoli, L., Cristau, B., Gouezo, F., and Fabre, C., *Chim. Anal.*, **45**, 439 (1963); *Chem. Abstr.*, **60**, 1335 (1964).
- (564) Vignoli, L., Cristau, B., Gouezo, F., and Fabre, C., *Chim. Anal.*, **45**, 499 (1963); *Chem. Abstr.*, **60**, 4806 (1964).
- (565) Visser, K., French Patent 1,328,137 (May 24, 1963); *Chem. Abstr.*, **60**, 2954 (1964).
- (566) Visser, K., French Patent 1,379,606 (Nov 27, 1964); *Chem. Abstr.*, **62**, 16261 (1965).
- (567) Visser, K., and Auke de Hoop, Dutch Patent 296,792 (May 25, 1965); *Chem. Abstr.*, **63**, 18092 (1965).
- (568) Vitalis, E. A., U. S. Patent 2,874,124 (Feb 17, 1959); *Chem. Abstr.*, **53**, 8670 (1959).
- (569) Wahl, W. W., U. S. Patent 3,116,264 (Dec 31, 1963); *Chem. Abstr.*, **60**, 7782 (1964).
- (570) Wakasa, R., and Shibata, K., Japanese Patent 7493 (May 30, 1963); *Chem. Abstr.*, **59**, 8900 (1963).
- (571) Walles, W. E., *Am. Chem. Soc., Div. Polymer Chem., Preprints*, **1**, 161 (1960); *Chem. Abstr.*, **57**, 4833 (1962).
- (572) Walles, W. E., U. S. Patent 3,065,130 (Nov 20, 1962); *Chem. Abstr.*, **58**, 7793 (1963).
- (573) Walles, W. E., U. S. Patent 3,079,396 (Feb 26, 1963); *Chem. Abstr.*, **59**, 2824 (1963).
- (574) Walles, W. E., U. S. Patent 3,080,344 (March 5, 1963); *Chem. Abstr.*, **58**, 14140 (1963).
- (575) Walles, W. E., U. S. Patent 3,179,667 (April 20, 1965); *Chem. Abstr.*, **63**, 1789 (1965).
- (576) Walles, W. E., Bakke, W. W., and Tousignant, W. F., U. S. Patent 3,157,641 (Nov 17, 1964); *Chem. Abstr.*, **62**, 2778 (1965).
- (577) Walles, W. E., Francis, W., and Houtman, T., Jr., German Patent 1,122,258 (Jan 18, 1962); *Chem. Abstr.*, **58**, 14145 (1963).
- (578) Walles, W. E., and Tousignant, W. F., U. S. Patent 2,872,321 (Feb 3, 1959); *Chem. Abstr.*, **53**, 8534 (1959).
- (579) Walles, W. E., and Tousignant, W. F., U. S. Patent 2,946,772 (July 26, 1960); *Chem. Abstr.*, **54**, 26014 (1960).
- (580) Walles, W. E., and Tousignant, W. F., U. S. Patent 2,948,708 (Aug 9, 1960); *Chem. Abstr.*, **54**, 26011 (1960).
- (581) Walles, W. E., and Tousignant, W. F., U. S. Patent 3,054,764 (Sept 18, 1962); *Chem. Abstr.*, **58**, 633 (1963).
- (582) Walles, W. E., and Tousignant, W. F., U. S. Patent 3,087,804 (April 30, 1963); *Chem. Abstr.*, **59**, 1038 (1963).
- (583) Walles, W. E., Tousignant, W. F., and Axelson, R. J., U. S. Patent 3,097,048 (July 9, 1963); *Chem. Abstr.*, **59**, 8929 (1963).
- (584) Walles, W. E., Tousignant, W. F., and Cloninger, L. C., U. S. Patent 3,067,143 (Dec 4, 1962); *Chem. Abstr.*, **58**, 10412 (1963).
- (585) Walles, W. E., Tousignant, W. F., and Cloninger, L. C., U. S. Patent 3,097,046 (July 9, 1963); *Chem. Abstr.*, **59**, 8929 (1963).
- (586) Walles, W. E., Tousignant, W. F., and Houtman, T., Jr., U. S. Patent 2,891,08 (June 16, 1959); *Chem. Abstr.*, **54**, 2359 (1960).
- (586a) Walles, W. E., Tousignant, W. F., and Houtman, T., Jr., U. S. Patent 2,919,279 (Dec 29, 1959); *Chem. Abstr.*, **54**, 21131 (1960).
- (587) Walles, W. E., Tousignant, W. F., and Houtman, T., *Am. Chem. Soc., Div. Polymer Chem., Preprints*, **1**, 58 (1960); *Chem. Abstr.*, **57**, 4858 (1962).
- (588) Weickmann, A., German Patent 858,402 (Dec 8, 1952); *Chem. Abstr.*, **47**, 11255 (1953).
- (589) Wein, J., *Acta Chim. Acad. Sci. Hung.*, **17**, 189 (1958); *Chem. Abstr.*, **55**, 5407 (1961).
- (590) Wein, J., *Acta Chim. Acad. Sci. Hung.*, **17**, 181 (1958); *Chem. Abstr.*, **55**, 4407 (1961).
- (591) Weinberg, A. E., *Dissertation Abstr.*, **16**, 1590 (1956).
- (592) Weiner, M. L., *J. Org. Chem.*, **26**, 951 (1961).
- (593) Werner, J., U. S. Patent 2,987,505 (Appl. March 4, 1958); *Chem. Abstr.*, **56**, 549 (1962).
- (594) Werner, J., U. S. Patent 3,148,123 (Sept 8, 1964); *Chem. Abstr.*, **61**, 13139 (1964).
- (595) Werner, J., and Hessel, F. A., U. S. Patent 3,097,087 (July 9, 1963); *Chem. Abstr.*, **59**, 9252 (1963).
- (596) Wilson, L. H., and Yun H., U. S. Patent 2,901,391 (Aug 25, 1959); *Chem. Abstr.*, **54**, 896 (1960).
- (597) Wirth, A. R., Messer, A. S., and Partansky, A. M., U. S. Patent 2,931,694 (April 5, 1960); *Chem. Abstr.*, **54**, 15946 (1960).
- (598) Wood, T. F., U. S. Patent 2,617,825 (Nov 11, 1952); *Chem. Abstr.*, **47**, 11255 (1953).
- (599) Wright, W. B., *J. Heterocyclic Chem.*, **2**, 41 (1965).
- (600) Yamada, S., Terashima, S., and Achiwa, K., *Chem. Pharm. Bull.*, **13**, 751 (1965); *Chem. Abstr.*, **63**, 8164 (1965).
- (601) Yeary, R. A., Benish, R. A., Brahm, C. A., and Miller, D. L., *Toxicol. Appl. Pharmacol.*, **6**, 642 (1964); *Chem. Abstr.*, **62**, 9673 (1965).
- (602) Yoshihara, K., Onodera, N., and Ikari, N., Japanese Patent 8731 (June 26, 1961); *Chem. Abstr.*, **60**, 9388 (1964).
- (603) Yurchenco, J. A., Yurchenco, M. C., and Piepoli, C. R., *Antibiot. Chemotherapy*, **3**, 1035 (1953); *Chem. Abstr.*, **48**, 8862 (1954).
- (604) Zajeva, S., Aleksejava, L., Ratenbergs, S., Koptelova, M. N., Medne, K., and Spure, I., *Zh. Mikrobiol. Epidemiol. i Immunobiol.*, **29**, 15 (1958); *Chem. Abstr.*, **52**, 20682 (1958).
- (605) Zangaglia, O., and Fantoni, S., *Giorn. Ital. Chemioterap.*, **5-9**, 33 (1962); *Chem. Abstr.*, **57**, 15607 (1962).
- (606) Zenisek, Z., and Petkova, R., *Sb. Cesk. Akad. Zemedel. ved, Zivocisna Vyroba*, **5**, 67 (1960); *Chem. Abstr.*, **55**, 1836 (1961).
- (607) Zhalyazkov, P., and Zikolova, Sv., *Farmatsiya* (Sofia), **13**, 24 (1963); *Chem. Abstr.*, **60**, 2816 (1964).
- (608) Zhelyazkov, L., Zikolova, Sv., and Bikova, N., *Farmatsiya* (Sofia), **7**, 19 (1957); *Chem. Abstr.*, **54**, 13102 (1960).
- (609) Zikolova, Sv., and Zhelyazkov, L., *Tr. Nauchno-Izled. Inst. Farm.*, **3**, 14 (1961); *Chem. Abstr.*, **61**, 9485 (1964).
- (610) Zikolova, Sv., and Zhelyazkov, L., *Farmatsiya* (Sofia), **14**, 16 (1964); *Chem. Abstr.*, **62**, 13135 (1965).
- (611) Zimmerman, H. E., and Traxler, M. D., *J. Am. Chem. Soc.*, **79**, 1920 (1957).
- (612) Zyzynski, W., *Acta Polon. Pharm.*, **18**, 365 (1961); *Chem. Abstr.*, **56**, 8846 (1962).

IX. ADDENDUM

In the period from January 1, 1966, to May 23, 1966, the following references have come to our attention. The designations in parentheses refer to the related section or sections in the present paper.

It is noteworthy that Hickner and Bolme claim to have alkylated the 2-oxazolidone ring at nitrogen by use of alkylene oxides in the presence of strong base. This is the first reported instance of such a reaction.

Gulbins and Hamann report the synthesis of 2-oxazolidones from cyclic ethylene carbonates and aromatic amines or diacyl-substituted ureas. In both cases lithium chloride catalyzes the reaction; in the former case, potassium or sodium hydroxide may also be used.

In two patents Ham reports the synthesis of 2-oxazolidones by rearrangement of 2-alkoxy-2-oxazolines in inert solvents with catalytic amounts of alkyl halides.

- (A1) Asta-Werke Akt.-Ges., Chemische Fabrik, Dutch Patent 6,400,655 (July 29, 1965); *Chem. Abstr.*, **64**, 5100 (1966) (IID).
- (A2) Brendel, K., Gross, P. H., and Zimmerman, H. K., Jr., *Ann.*, **691**, 192 (1966) (IIIA1, IIIC4).
- (A3) Cervi, F. R., Hauser, M., Sprague, G. S., and Troffkin, H. J., *J. Org. Chem.*, **31**, 631 (1966) (IIIA3, IVB).
- (A4) Forgione, P. S., Sprague, G. S., and Troffkin, H. J., *J. Am. Chem. Soc.*, **88**, 1079 (1966) (IIIC1).
- (A5) Gulbins, E., and Hamann, K., *Ber.*, **99**, 55 (1966) (II-I).
- (A6) Gulbins, E., and Hamann, K., *Ber.*, **99**, 62 (1966) (IIH4, II-I).
- (A7) Ham, G. E., U. S. Patent 3,214,435 (Oct 26, 1965); *Chem. Abstr.*, **64**, 3544 (1966) (IIQ).
- (A8) Ham, G. E., U. S. Patent 3,231,578 (Jan 25, 1966); *Chem. Abstr.*, **64**, 9731 (1966) (IIQ, IVA4).
- (A9) Hauser, M., *J. Org. Chem.*, **31**, 968 (1966) (IIK2, IIIC1).
- (A10) Hickner, R. A., U. S. Patent 3,221,021 (Nov 30, 1965); *Chem. Abstr.*, **64**, 6657 (1966) (IIIB2).
- (A11) Hickner, R. A., U. S. Patent 3,228,955 (Jan 11, 1966); *Chem. Abstr.*, **64**, 8187 (1966) (IIIC3, IVC).
- (A12) Hickner, R. A., and Bolme, D. W., U. S. Patent 3,242,187 (March 22, 1966); *Chem. Abstr.*, **64**, 15890 (1966) (IIIB).
- (A13) Irikura, T., and Masuzawa, K., Japanese Patent 24,458 (Oct 26, 1965); *Chem. Abstr.*, **64**, 5100 (1966) (IIF1,2; IVA4).
- (A14) Irikura, T., and Masuzawa, K., Japanese Patent 1947 (Feb 10, 1966); *Chem. Abstr.*, **64**, 14193 (1966) (IIB1, VIIA4).
- (A15) Iwakura, Y., and Izawa, S., *Yuki Gosei Kagaku Kyokai Shi*, **24**, 60 (1966); *Chem. Abstr.*, **64**, 8163 (1966) (IIH5).
- (A16) Iwakura, Y., Izawa, S., and Hayano, F., *J. Polymer Sci.*, **A4**, 751 (1966) (IIH5, IVB).
- (A17) Kulkarni, S. R., *Dissertation Abstr.*, **26**, 2477 (1965); *Chem. Abstr.*, **64**, 6731 (1966) (IIT).
- (A18) Misiiti, D., Amato, A., and Rosnati, V., *Ann. Ist. Super. Sanita*, **1**, 222 (1965); *Chem. Abstr.*, **64**, 3513 (1966) (IIB1,6).
- (A19) Phillips, B. L., and Argabright, P. A., *J. Heterocyclic Chem.*, **3**, 84 (1966) (IIE4).
- (A20) Pomot, J. L., U. S. Patent 3,215,701 (Nov 2, 1965); *Chem. Abstr.*, **64**, 2089 (1966) (IIB4, IIIB3,4).
- (A21) Regnier, G., Canevari, R., and LeDourarec, J.-C., French Patent 1,395,085 (April 9, 1965); *Chem. Abstr.*, **64**, 2090 (1966) (IIIC4).
- (A22) Science Union et Cie.-Société Française de Recherche Medicale, Dutch Patent 6,504,602 (Oct 25, 1965); *Chem. Abstr.*, **64**, 12679 (1966) (IIB2, IVA4).
- (A23) Tousignant, W. F., and Sovich, R. C., U. S. Patent 3,226,372 (Dec 28, 1965); *Chem. Abstr.*, **64**, 8187 (1966) (IIB1, IVB).
- (A24) Upjohn Co., Dutch Patent Appl. 6,505,537 (Nov 2, 1965); *Chem. Abstr.*, **64**, 15812 (1966) (IIB1).
- (A25) Walles, W. E., U. S. Patent 3,231,577 (Jan 25, 1966); *Chem. Abstr.*, **64**, 9731 (1966) (IIH1).