2-OXAZOLIDONES

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Received June 22, 1966

CONTENTS

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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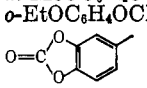
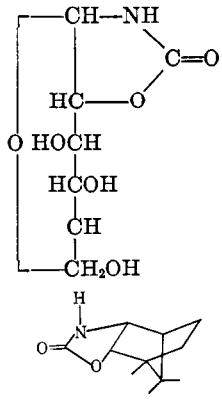
TABLE I

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
$C_3H_5NO_2$	H	H	H	H	H	89	60	464, 545
$C_5H_7NO_4$	H	HOOC	H	Me	H	196–197 dec (DL-*cis*)	26	283, 285, 377
$C_5H_9NO_3$	$HOCH_2CH_2$	H	H	H	H	161 (0.1)	50	544
$C_6H_9NO_4$	EtOCO	H	H	H	H	51–52 (EtOAc–heptane)	95	50
$C_6H_9NO_4$	CH_2=$CHCH_2OCO$	H	H	H	H	41–42 (EtOAc–heptane)	90	50
$C_6H_{11}NO_4$	*n*-PrOCO	H	H	H	H	53–54 (EtOAc–heptane)	92	50
$C_7H_{11}NO_2$	H	H	—$(CH_2)_4$—		H	*trans*, 99–100 ($CHCl_3$–pet. ether); 100–102; 100–110 (0.01)	80	357, 358
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	H	H	255	62	205
$C_8H_{12}NO_2Cl$	H	H	H	—$(CH_2)_2$CH(Cl)$(CH_2)_2$—		150	..	434
$C_8H_{13}NO_2$	H	H	—$(CH_2)_4$—		Me	*trans*, 107–109 (Et_2O–pet. ether)	50	358
$C_9H_9NO_2$	H	H	H	Ph	H	87–87.5 (EtOH–hexane)	96	426
$C_{10}H_{10}N_2O_6$	*p*-$O_2NC_6H_4CH_2$	H	H	H	H	171–173 (EtOAc–hexane)	82	50
$C_{10}H_{11}NO_2$	*m*-MeC_6H_4	H	H	H	H	...	..	109
	p-MeC_6H_4	H	H	H	H	...	..	109
$C_{11}H_{11}NO_4$	$PhCH_2OCO$	H	H	H	H	101–102 (EtOAc–heptane)	89	50
$C_{11}H_{12}NO_4Cl$	H	H	H	*o*-$ClC_6H_4OCH_2$	H	73.5	..	12
	H	H	H	*m*-$ClC_6H_4OCH_2$	H	79–81	..	12
$C_{11}H_{13}NO_3$	H	H	H	*o*-$MeC_6H_4OCH_2$	H	128–129 (EtOAc)	..	44
$C_{11}H_{13}NO_4$	H	H	H	*o*-$MeOC_6H_4OCH_2$	H	141–142 (H_2O)	37	12, 322
	H	H	H	*m*-$MeOC_6H_4OCH_2$	H	121–123	..	12
$C_{12}H_{13}NO_3Cl_2$	Et	H	H	2,4-$Cl_2C_6H_3OCH_2$	H	215–220 (0.12)	20	325
$C_{12}H_{14}NO_3Cl$	Et	H	H	*p*-$ClC_6H_4OCH_2$	H	116–117	99	325
$C_{12}H_{14}NO_3Br$	Et	H	H	*p*-$BrC_6H_4OCH_2$	H	122.5	98	325
$C_{12}H_{15}NO_3$	Et	H	H	$PhOCH_2$	H	43–44 (*i*-Pr_2O), 182–185 (0.15)	77	325
$C_{12}H_{15}NO_4$	Me	H	H	*o*-$MeOC_6H_4OCH_2$	H	77.5–78.5 (*i*-Pr_2O), 180–195 (0.08)	73	12, 325
	Me	H	H	*p*-$MeOC_6H_4OCH_2$	H	...	..	12
	Me	H	H	*m*-$MeOC_6H_4OCH_2$	H	73.5	..	12
	H	H	H	*o*-$EtOC_6H_4OCH_2$	H	98–100	..	12
$C_{13}H_{13}NO_5$	*i*-Pr	H	H		H	106–107 (C_6H_6–hexane)	..	520
$C_{13}H_{16}NO_3Cl$	Et	H	H	4-Cl-3-$MeC_6H_3OCH_2$	H	94–94.5 (isooctane)	82	325
	Et	H	H	3-Cl-2-$MeC_6H_3OCH_2$	H	115–116	85	325
	Et	H	H	5-Cl-2-$MeC_6H_3OCH_2$	H	77 (*i*-Pr_2O)	45	325
$C_{13}H_{17}NO_3$	Et	H	H	*o*-$MeC_6H_4OCH_2$	H	50–50.5 (*i*-Pr_2O)	59	325
	Et	H	H	*m*-$MeC_6H_4OCH_2$	H	50–51	40	325
	Et	H	H	*p*-$MeC_6H_4OCH_2$	H	90–91 (*i*-Pr_2O)	52	325
$C_{13}H_{17}NO_4$	Et	H	H	*p*-$MeOC_6H_4OCH_2$	H	80–81 (*i*-Pr_2O)	96	325
	Et	H	H	*o*-$MeOC_6H_4OCH_2$	H	175–178 (0.1)	..	12
$C_{14}H_{19}NO_3$	Et	H	H	2,4-$Me_2C_6H_3OCH_2$	H	37–38.5 (*i*-Pr_2O)	56	325
	Et	H	H	3,5-$Me_2C_6H_3OCH_2$	H	71–72 (*i*-Pr_2O), 204–205 (0.08)	..	325
$C_{14}H_{19}NO_4$	*i*-Pr	H	H	*o*-$MeOC_6H_4OCH_2$	H	76–78 (*i*-Pr_2O)	28	325
$C_{15}H_{13}NO_2$	H	Ph	H	Ph	H	*trans*, 159–160; *cis*, 188–189	..	262
$C_{15}H_{21}NO_3$	Et	H	H	2,3,5-$Me_3C_6H_2OCH_2$	H	154–155 (EtOAc)	14	325
$C_{15}H_{21}NO_4$	*n*-Bu	H	H	*o*-$MeOC_6H_4OCH_2$	H	186–188 (0.03)	76	325
$C_{16}H_{15}NO_2$	Me	Ph	H	Ph	H	*trans*, 90; *cis*, 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
$C_{22}H_{19}NO_2$	*m*-MeC_6H_4	Ph	H	Ph	H	189 (EtOH)	..	109
	p-MeC_6H_4	Ph	H	Ph	H	209 (EtOH)	..	109

Structure	Mp, °C	Ref
	220–222 dec (70% aq MeOH) tetraacetyl deriv, 150–151	501
	123 (Et_2O) (51% yield)	224

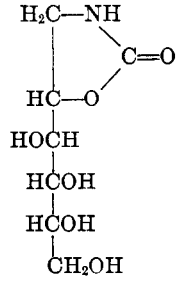
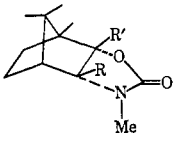
Structure	Mp, °C	Ref
	155–156 tetraacetyl deriv, 126–127	501

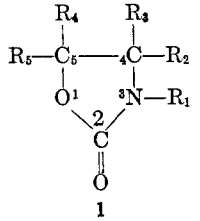
TABLE I (*Continued*)



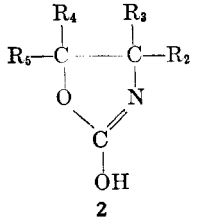
Camphane Derivatives (224)

R	R′	Mp or bp (mm), °C	% yield
H	Cl	82 (Et_2O–hexane)	70
HO	H	193 (MeOH–Et_2O)	80
HO	D	192–193	..
H	H	119 (Et_2O)	60
H	MeO	122	60
H	EtO	145 (0.07)	90
H	AcO	107 (hexane)	87
H	$PhCH_2O$	153–154	87
AcO	H	120.5 (Et_2O)	85
Cl	Cl	132 (Et_2O–hexane)	80
HO	Cl	254 dec (MeOH–Et_2O)	100
AcO	Cl	84–85 (Et_2O–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 R_1 = H (2).



1



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

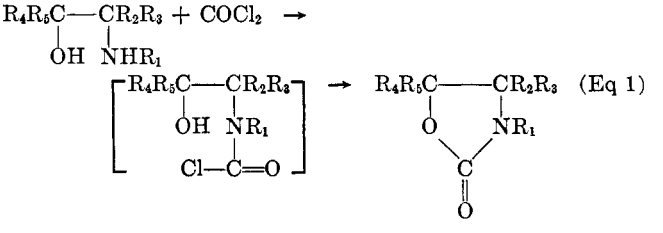
A. INTRODUCTION

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

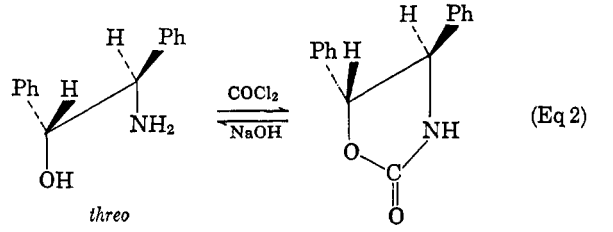
1. Using Phosgene (Table I)

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.



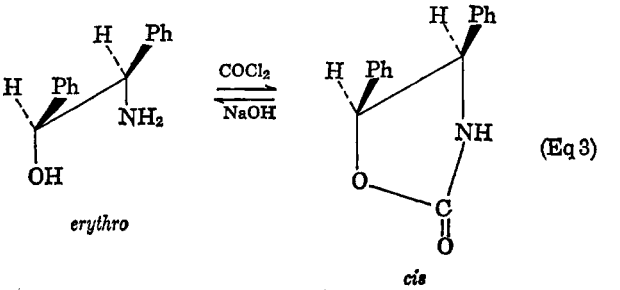
(Eq 1)

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



(Eq 2)

threo *trans*



(Eq 3)

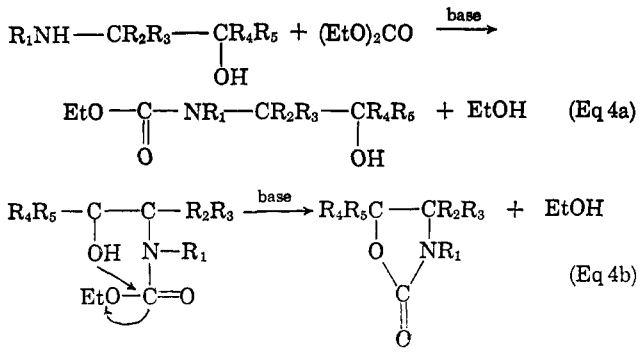
erythro *cis*

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.

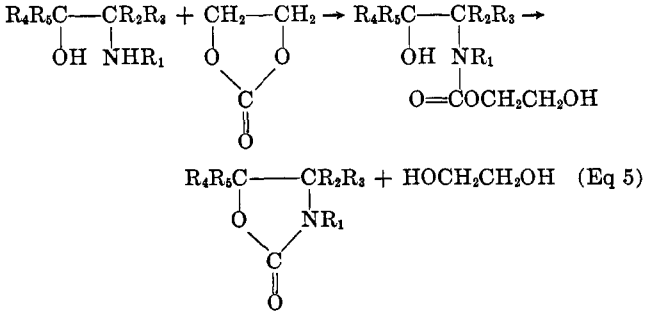
Although the reaction might be looked upon as the generation of carbon dioxide *in situ* with its subsequent addition to the alcohol–amine system, accompanied by the elimination of the elements of water (*cf.* next section), the evidence suggests that the reaction proceeds in two stages (248): first, 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.



(Eq 4a)

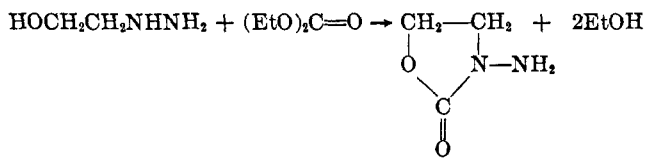
(Eq 4b)

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).



(Eq 5)

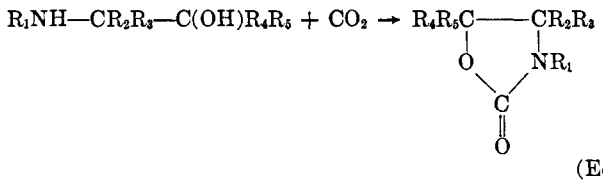
Although the R_1–N bond is usually a carbon–nitrogen bond, it may also be a nitrogen–nitrogen bond. The amino alcohol starting material is then a β-hydroxyhydrazine (197, 388, 423, 528, 529, 565) (Eq 6). The products are 3-amino-2-oxazolidones.



(Eq 6)

3. *Using Carbon Dioxide (Table III)*

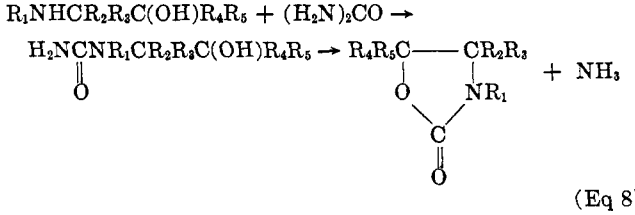
Gaseous carbon dioxide has been used to produce 2-oxazolidones from β-amino alcohols in a limited number of cases described only in patents. The reactions are carried out with or without solvent at elevated temperatures under pressure (Eq 7). The reaction has the advantage of simplicity, but it has not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



(Eq 7)

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).



(Eq 8)

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 ephedrines (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

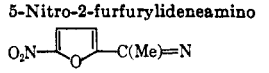
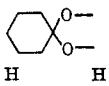
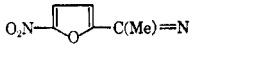
Empirical formula	R_1	R_2	R_3	R_4	R_5	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	H	H	H	87–89 ($CHCl_3$), 90–91 (ligroin), 170–172 (3)	67	147, 250, 326, 560
$C_3H_6N_2O_2$	H_2N	H	H	H	H	69–71 (EtOH), 70.5–71	93	195, 389, 528
$C_4H_4NO_2Cl_3$	H	H	H	Cl_3C	H	125–125.5 (Me_2CO–EtOH)	...	74
$C_4H_7NO_2$	H	H	H	Me	H	111–113 (1)	...	48, 371
	Me	H	H	H	H	15, 87–90 (1)	...	48
$C_4H_7NO_3$	H	H	H	$HOCH_2$	H	...	...	13
$C_4H_8N_2O_2$	H_2N	Me	H	H	H	...	36	205
	H_2N	H	H	Me	H	50.3–50.5	70	195, 205, 389
$C_4H_8N_2O_3$	H_2N	$HOCH_2$	H	H	H	...	34	205
	H_2N	H	H	$HOCH_2$	H	156–157 ...	...	195, 227, 389
$C_5H_7NO_2Cl_2$	H	$ClCH_2$	$ClCH_2$	H	H		...	461
$C_5H_8NO_2Cl$	$ClCH_2CH_2$	H	H	H	H	137–138 (3)	...	121
$C_5H_8NO_2I$	ICH_2CH_2	H	H	H	H	...	...	121
$C_5H_8N_2O_3$	CH_3CONH	H	H	H	H	93–94 (EtOH)	95	529
$C_5H_9NO_2$	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
$C_5H_9NO_3$	$HOCH_2CH_2$	H	H	H	H	164–166 (1)	...	48, 250
	H	Me	$HOCH_2$	H	H	115–116.5 (EtOH), 120 (EtOH–C_6H_6)	61	248, 250, 417
$C_5H_9NO_4$	H	$HOCH_2$	$HOCH_2$	H	H	109–110 (Me_2CO, then EtOH)	...	250
$C_5H_{10}N_2O_2$	H_2N	Me	Me	H	H	130–135 (10)	...	389
	H_2N	Me	H	Me	H	...	45	195, 205, 389
	H_2N	H	H	Et	H	...	20	205
	H_2N	Et	H	H	H	...	62	205
$C_5H_{10}N_2O_2S$	H_2N	H	H	$MeSCH_2$	H	...	...	423
$C_6H_9NO_4$	H	—OCMe$_2$O—		H	H	164–165 (EtOAc)	62	461
$C_6H_{10}NO_2Cl$	$Cl(CH_2)_3$	H	H	H	H	156 (3)	...	121
$C_6H_{10}NO_2I$	$I(CH_2)_3$	H	H	H	H	...	...	121
$C_6H_{10}N_2O_2$	$Me_2C{=}N$	H	H	H	H	110–115 (5)	...	565
$C_6H_{11}NO_2$	H	Me	H	*n*-Pr	H	133 (1.5)	...	250
$C_6H_{11}NO_3$	H	H	H	$HOCH_2$	Et	...	...	13
$C_6H_{12}N_2O_2$	H_2N	*n*-Bu	H	H	H	135 (0.7)	46	195, 205, 389
	H_2N	H	H	*n*-Bu	H	...	42	205
$C_7H_{13}NO_2$	*n*-Bu	H	H	H	H	98.2–99.3 (0.5), 94 (1)	...	147, 250
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	H	H	256–257 (DMF)	...	205, 274, 388, 523
$C_8H_{13}NO_2$	H	—$(CH_2)_5$—		H	H	81–82	89	156, 382
$C_8H_{14}NO_3Cl$	H	H	H	2-Me-5-Cl-$C_6H_3OCH_2$	H	77	45	319
$C_8H_{16}N_2O_2$	H_2N	H	H	N-Pyrrolidinomethyl	H	163–167 (2.5)	...	199
$C_8H_{16}N_2O_3$	H_2N	H	H	N-Morpholinomethyl	H	120 (*i*-PrOH)	...	200, 203, 227
$C_8H_{16}N_2O_2$	H	H	H	Et_2NCH_2	H	51.5–53 (EtOH)	88.5	478
$C_8H_{17}N_2O_2I$	$Me_3N^+CH_2CH_2$ I^-	H	H	H	H	227	...	121
$C_8H_{17}N_3O_2$	H_2N	H	H	Et_2NCH_2	H	170–171, 138.5 (1.6)	...	200, 203
$C_9H_8N_3O_5Cl$	5-Nitro-2-furfurylideneamino	H	H	$ClCH_2$	H	195–196	...	205, 388
$C_9H_9NO_2$	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
$C_9H_9N_3O_5$	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
$C_9H_9N_3O_6$	5-Nitro-2-furfurylideneamino	H	H	$HOCH_2$	H	241–243	...	205, 388
$C_9H_{13}NO_4$	H			H	H	201–202 (Me_2CO)	...	461
$C_9H_{15}NO_2$	Cyclohexyl	H	H	H	H	33–34, 151–153 (4), 128–131 (0.5–1.0)	...	560, 598
$C_9H_{17}N_3O_2$	H_2N	H	H	N-Piperidinomethyl	H	128–129	44	200, 203
$C_9H_{18}N_2O_3$	H	$HOCH_2$	Et_2NCH_2	H	H	51–54 (pentane), 205–210 (0.08)	54	461
$C_9H_{19}N_2O_2I$	$Me_3N^+(CH_2)_3$ I^-	H	H	H	H	123	...	121
$C_{10}H_8NO_3Cl_3$	H	H	H	2,4,6-$Cl_3C_6H_2OCH_2$	H	...	...	319
$C_{10}H_9NO_3Cl_2$	H	H	H	2,4-$Cl_2C_6H_3OCH_2$	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
$C_{10}H_{11}N_3O_5$	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*)

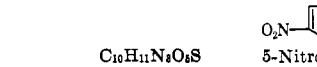
Empirical formula	R_1	R_2	R_3	R_4	R_5	Bp (mm) or mp, °C	% yield	Ref
		H	H	H	H	102	...	205
		H	H	H	H	132–135	...	388
$C_{10}H_{11}N_3O_6S$	5-Nitro-2-furfurylideneamino	H	H	$MeSCH_2$	H	182 (HOAc)	...	423
$C_{10}H_{11}N_3O_7S$	5-Nitro-2-furfurylideneamino	H	H	$MeSO_2CH_2$	H	195	...	423
$C_{10}H_{13}NO_4$	H	H	H	*o*-$MeOC_6H_4OCH_2$	H	140.5–142.0 (EtOH)	...	323
$C_{10}H_{16}NO_3Cl$	H	H	H	2-Pr-6-$ClC_6H_3OCH_2$	H	...	...	319
$C_{10}H_{16}NO_4Cl$	H	H	H	2-PrO-6-$ClC_6H_3OCH_2$	H	...	...	319
$C_{10}H_{17}NO_2$	$PhCH_2$	H	H	H	H	78–80 (pet. ether–C_6H_6)	91	598
$C_{11}H_{11}NO_3F$	H	H	H	2-Me-4-$FC_6H_3OCH_2$	H	...	...	319
$C_{11}H_{11}NO_3Br$	H	H	H	2-Me-4-$BrC_6H_3OCH_2$	H	...	...	319
$C_{11}H_{11}N_2O_2Cl$	$PhCH{=}N$	H	H	$ClCH_2$	H	117.5–118 (abs. EtOH)	...	227
$C_{11}H_{11}N_3O_6S$	5-Nitro-2-furfurylideneamino	H	H	$CH_2{=}CHSCH_2$	H	150	...	423
$C_{11}H_{12}N_2O_3$	$PhCH{=}N$	H	H	$HOCH_2$	H	138–138.5 (abs. EtOH)	...	227
$C_{11}H_{13}NO_2$	Me	Me	H	Ph	H	92–92.5 (C_6H_6–pet. ether)	89	250
$C_{11}H_{13}N_3O_7S$	5-Nitro-2-furfurylideneamino	H	H	$EtSO_2CH_2$	H	159	...	423
$C_{11}H_{16}N_2O_2$	H_2N	H	H	$PhMeNCH_2$	H	214–215	...	200
$C_{11}H_{18}NO_3Cl$	Pr	H	H	2-Me-3-$ClC_6H_3OCH_2$	H	...	...	319
$C_{11}H_{19}N_3O_3$	$Me_2C{=}N$	H	H	N-Morpholinomethyl	H	172–175 (1–2)	75	567
$C_{11}H_{23}N_2O_2I$	$Et_3N^+CH_2CH_2I^-$	H	H	H	H	116	...	121
$C_{12}H_{13}NO_3Cl_2$	Et	H	H	2,4-$Cl_2C_6H_3OCH_2$	H	215–220 (0.12)	20	325
$C_{12}H_{13}N_3O_6S$	5-Nitro-2-furfurylideneamino	H	H	$CH_2{=}CHCH_2SCH_2$	H	118	...	423
$C_{12}H_{15}NO_3$	H	H	H	2,6-$Me_2C_6H_3OCH_2$	H	117.0–118.5	...	319
	Et	H	H	$PhOCH_2$	H	43–44 (*i*-Pr_2O), 182–185 (0.15)	77	325
$C_{12}H_{15}NO_3Cl$	Et	H	H	*p*-$ClC_6H_4OCH_2$	H	116–117	99	325
$C_{12}H_{15}NO_3Br$	Et	H	H	*p*-$BrC_6H_4OCH_2$	H	122.5	98	325
$C_{12}H_{15}NO_4$	Me	H	H	*o*-$MeOC_6H_4OCH_2$	H	77.5–78.5 (*i*-Pr_2O), 73–75, 180–195 (0.08)	73	321
$C_{12}H_{15}NO_5$	H	H	H	2,6-$(MeO)_2C_6H_3OCH_2$	H	104–105, 117–118.5	...	319, 321
$C_{12}H_{16}N_2O_3$	5-Nitro-2-furfurylideneamino	Bu	H	H	H	150–151	...	205, 388
	5-Nitro-2-furfurylideneamino	H	H	Bu	H	194	...	205, 388
$C_{12}H_{16}N_3O_6S$	5-Nitro-2-furfurylideneamino	H	H	*n*-$PrSCH_2$	H	148	...	423
	5-Nitro-2-furfurylideneamino	H	H	*i*-$PrSCH_2$	H	170	...	423
$C_{12}H_{16}N_3O_7S$	5-Nitro-2-furfurylideneamino	H	H	*n*-$PrSO_2CH_2$	H	158	...	423
	5-Nitro-2-furfurylideneamino	H	H	*i*-$PrSO_2CH_2$	H	180	...	423
$C_{12}H_{28}N_2O_2I$	$Et_3N^+(CH_2)_3$ I^-	H	H	H	H	131	...	121
$C_{12}H_{28}N_2O_2$	H_2N	H	H	Bu_2NCH_2	H	152.5–153.5	...	200
$C_{13}H_{16}NO_4Cl$	Et	H	H	3-Cl-2-$MeC_6H_3OCH_2$	H	110–111, 115–116	85	319, 325
	Et	H	H	4-Cl-3-$MeC_6H_3OCH_2$	H	94–94.5 (isooctane)	82	325
	Et	H	H	5-Cl-2-$MeC_6H_3OCH_2$	H	77 (*i*-Pr_2O)	45	325
$C_{13}H_{16}N_4O_6$	5-Nitro-2-furfurylideneamino	H	H	N-Morpholinomethyl	H	169.5–170.5 (EtOH) (D form) 208–209 (*i*-PrOH–$MeNO_2$) (L form)	...	227
$C_{13}H_{17}NO_3$	Et	H	H	*o*-$MeC_6H_4OCH_2$	H	50–50.5 (*i*-Pr_2O)	59	325
	Et	H	H	*m*-$MeC_6H_4OCH_2$	H	50–51	40	325
	Et	H	H	*p*-$MeC_6H_4OCH_2$	H	90–91 (*i*-Pr_2O)	52	325
$C_{13}H_{17}NO_4$	Et	H	H	*p*-$MeOC_6H_4OCH_2$	H	80–81 (*i*-Pr_2O)	96	325
$C_{13}H_{17}N_2O_2$	Et	H	H	*p*-$MeC_6H_4NHCH_2$	H	67–68 (ligroin–C_6H_6)	91	314
$C_{13}H_{17}N_3O_6S$	5-Nitro-2-furfurylideneamino	H	H	*n*-$BuSCH_2$	H	134	...	423
$C_{13}H_{17}N_3O_7S$	5-Nitro-2-furfurylideneamino	H	H	*n*-$BuSO_2CH_2$	H	150	...	423
$C_{14}H_{18}NO_3$	H	H	H	2,6-$Et_2C_6H_3OCH_2$	H	...	...	319
$C_{14}H_{18}N_2O_3$	*p*-MeC_6H_4	H	H	N-Morpholinyl	H	119.5–120.5 (ligroin–C_6H_6)	96	314
$C_{14}H_{18}N_4O_5$	5-Nitro-4-furfurylideneamino	H	H	N-Piperidinomethyl	H	197–198 (EtOH)	...	200
$C_{14}H_{18}N_4O_6$	5-Nitro-4-furfurylideneamino	H	H	2-Me-N-morpholinomethyl	H	174	...	168
$C_{14}H_{19}NO_3$	Et	H	H	2,4-$Me_2C_6H_3OCH_2$	H	37–38.5 (*i*-Pr_2O)	56	325
	Et	H	H	3,5-$Me_2C_6H_3OCH_2$	H	71–72 (*i*-Pr_2O), 202–205 (0.08)	42	325, 437
$C_{14}H_{19}NO_4$	*i*-Pr	H	H	*o*-$MeOC_6H_4OCH_2$	H	76–78 (*i*-Pr_2O)	28	325
$C_{14}H_{19}N_2O_2Cl$	*n*-Bu	H	H	*p*-$ClC_6H_4NHCH_2$	H	81.5–82.5 (ligroin–C_6H_6)	78	314
$C_{14}H_{20}N_2O_2$	*n*-Pr	H	H	*p*-$MeC_6H_4NHCH_2$	H	94–96 (ligroin–C_6H_6)	90	314
	n-Bu	H	H	$PhNHCH_2$	H	74–76 (Et_2O)	86	314
$C_{14}H_{21}N_2O_2I$	$(PhCH_2)Me_2N^+CH_2CH_2I^-$	H	H	H	H	170	...	121
$C_{15}H_{13}NO_2$	H	H	H	Ph	Ph	...	...	382
	H	Ph	Ph	H	H	178.4–178.8	98	156, 382
$C_{15}H_{16}N_2O_2$	H	N-Piperidinomethyl	N-Piperidinomethyl	H	H	180–181 (EtOH)	...	461
$C_{15}H_{18}N_4O_5$	5-Nitro-2-furfurylideneamino	H	H	$(CH_2{=}CHCH_2)_2NCH_2$	H	151	...	168
$C_{15}H_{19}N_3O_3$	$PhCH{=}N$	H	H	N-Morpholinomethyl	H	169.5–170.5 (EtOH)	...	227
$C_{15}H_{20}N_4O_6$	5-Nitro-2-furfurylideneamino	H	H	2,6-Me_2-N-morpholinomethyl	H	203	...	168
$C_{15}H_{20}N_6O_5$	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-$Me_3C_6H_2OCH_2$	H	154–155 (EtOAc)	14	325
$C_{15}H_{21}NO_4$	*n*-Bu	H	H	*o*-$MeOC_6H_4OCH_2$	H	186–188 (0.03)	76	325
$C_{15}H_{22}N_2O_2$	*n*-Bu	H	H	*p*-$MeC_6H_4NHCH_2$	H	73.5–74.5 (ligroin–C_6H_6)	96	314
	n-Bu	H	H	*m*-$MeC_6H_4NHCH_2$	H	55.5–56.5 (ligroin–C_6H_6)	94	314

TABLE II (*Continued*)

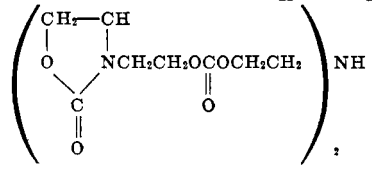
Empirical formula	R_1	R_2	R_3	R_4	R_5	Bp (mm) or mp, °C	% yield	Ref
$C_{16}H_{22}N_6O_8$	5-Nitro-2-furfurylideneamino	H	H	N-Et-N′-piperazinomethyl	H	193	...	168
	5-Nitro-2-furfurylideneamino	H	H	3,4-Me_2-N-piperazinomethyl	H	161–164	...	168
	5-Nitro-2-furfurylideneamino	H	H	2,4-Me_2-N-piperazinomethyl	H	191–193	...	168
$C_{16}H_{23}NO_5$	H	H	H	2,6-(*n*-PrO)$_2$$C_6H_3OCH_2$	H	...	...	319, 321
$C_{16}H_{23}N_2O_2$	*n*-Am	H	H	*p*-$MeC_6H_4NHCH_2$	H	81–82 (ligroin–C_6H_6)	92	314
$C_{16}H_{24}N_2O_2$	Ph	H	H	*n*-Bu_2NCH_2	H	32–33 (Et_2O–pet. ether)	87	314
$C_{17}H_{23}NO_4$	Cyclohexyl	H	H	*o*-$MeOC_6H_4OCH_2$	H	68–69	...	321
$C_{17}H_{25}N_5O_5$	5-Nitro-2-furfurylideneamino	H	H	N-*n*-Pr-N′-piperazinomethyl	H	184–185	...	168
$C_{18}H_{19}NO_4$	$PhCH_2$	H	H	*o*-$MeOC_6H_4OCH_2$	H	59–59.5 (isooctane–Et_2O)	70	321, 325
$C_{18}H_{20}N_2O_2$	*p*-MeC_6H_4	H	H	*p*-$MeC_6H_4NHCH_2$	H	157–158.5 (ligroin–C_6H_6)	87	314
$C_{18}H_{21}N_3O_2$	H_2N	H	H	$(PhCH_2)_2NCH_2$	H	163–165	...	200–203
$C_{20}H_{24}N_2O_2$	Ph	H	H	*n*-BuPhNCH$_2$	H	214–216 (1.5)	64	314
						106–108 (EtOH)	...	250

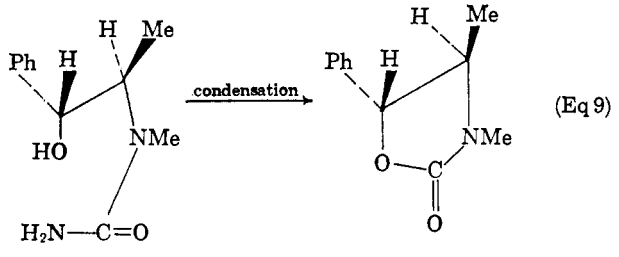
TABLE III

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

Empirical formula[a]	R_1	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	88–89 ($CHCl_3$)	35	326
$C_5H_9NO_2$	Me	Me	92 (1.5)	58	495
$C_6H_{11}NO_2$	Et	Me	87 (1)	..	495
$C_7H_{13}NO_3$	$CH_3CH(OH)CH_2$	Me	132–133 (0.2)	76	495
$C_8H_{15}NO_2$	Et	*i*-Pr	107 (1)	..	495

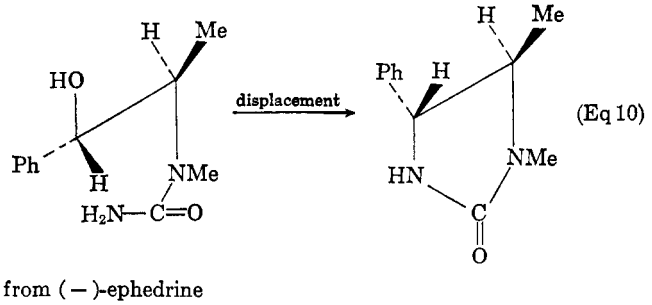
[a] $R_2 = R_3 = R_5 = H$.

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



(Eq 9)

from (+)-pseudoephedrine



(Eq 10)

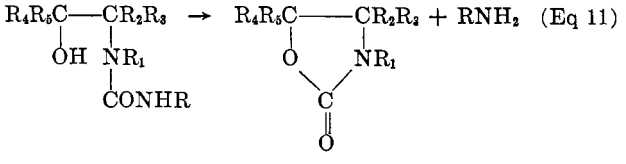
from (−)-ephedrine

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).

$$R_4R_5C(OH)C(NHR_1)R_2R_3 + RNCO \rightarrow$$



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-carbethoxy derivative (β-hydroxyurethan). This subsequently cyclizes with loss of ethanol (Eq 12).

TABLE IV

2-OXAZOLIDONES PREPARED FROM β-AMINO ALCOHOLS AND UREAS

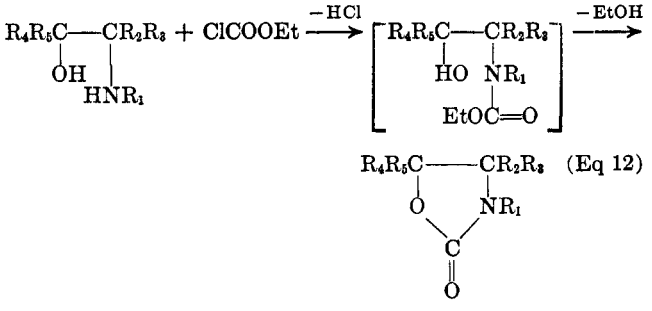
Empirical formula	R_1	R_2	R_3	R_4	R_5	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	H	H	H	85–87 ($CHCl_3$)	83	251
$C_4H_7NO_2$	Me	H	H	H	H	180 (1.5)	...	251
	H	H	H	Me	H	20–22, 110–111 (0.1–0.2)	...	57, 251, 481
$C_5H_9NO_2$	H	Me	Me	H	H	56.5–58 (EtOH–Et_2O)	13	97
	H	H	H	Me	Me	79–82 (EtOH–Skellysolve B)	53	97
$C_5H_9NO_3$	H	$HOCH_2$	Me	H	H	115 (MeOH, then Me_2CO)	73	251
$C_5H_9NO_4$	H	$HOCH_2$	$HOCH_2$	H	H	107–109 (EtOH)	69	251
$C_7H_{11}NO_2$	H	H	—$(CH_2)_4$—		H	*trans*, 100–102 ($CHCl_3$–pet. ether)	10	357, 358
$C_8H_7N_3O_5$	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*-Bu	Me	69–70 (EtOH–Skellysolve B)	60	97
	H	Me	Me	*i*-Pr	H	50–52 (Et_2O–Skellysolve B)	83	97
$C_{15}H_{13}NO_2$	H	Ph	H	Ph	H	*trans*, 159–160; *cis*, 188–190	73 (*t*)	261
	H	H	H	Ph	Ph	199–200 (EtOH)	82	97
$C_{16}H_{15}NO_2$	Me	Ph	H	Ph	H	*trans*, 90	...	261

TABLE V

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

Empirical formula[a]	R_1	R_3	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	H	90 (EtOH)	..	290
$C_6H_{11}NO_2$	H	Me	Et	143–144 (2)	53	588
$C_7H_{11}NO_2$	H	—$(CH_2)_4$—		*trans*, 100–102;	..	357
				cis, 55–56	..	357
$C_8H_{13}NO_2$	Me	—$(CH_2)_4$—		*trans*, 51–52;	..	357
				cis, liquid	..	357
$C_{10}H_{10}NO_3Cl$	H	H	*o*-$ClC_6H_4OCH_2$	151 (EtOAc)	..	44
$C_{15}H_{13}NO_2$	H	Ph	Ph	*cis*, 188–190	62	261, 262
$C_{16}H_{15}NO_2$	Me	Ph	Ph	*trans*, 90	..	261, 262

[a] $R_2 = R_5 = H$.

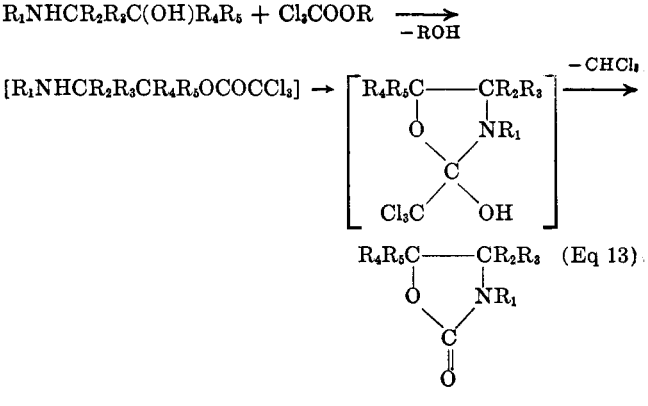


(Eq 12)

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).



(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
$C_3H_5NO_2$	H	H	H	H	87	60	562
$C_5H_7N_3O_3$	H	O_2NOCH_2	O_2NOCH_2	H	106–107	..	60
$C_5H_9NO_4$	H	$HOCH_2$	$HOCH_2$	H	109.5–110.7 (MeOH)	68	60, 90
$C_6H_{11}NO_2$	H	H	H	*i*-Pr	(D) 113–114 (C_6H_6–ligroin, then C_6H_6)	..	376
$C_8H_7N_3O_5$	2-Furfurylideneamino	H	H	H	173–174 (50% EtOH)	90	444
$C_9H_{13}NO_6$	H	$MeCOOCH_2$	$MeCOOCH_2$	H	69–70.4	..	90
$C_9H_{17}NO_3$	*i*-Bu	Me	$HOCH_2$	H	72–73, 121–122 (0.01)	53	351
$C_{10}H_{10}N_2O_2$	PhCH=N	H	H	H	143–145 (EtOH)	85	141, 205
$C_{10}H_{10}N_2O_4$	*p*-$O_2NC_6H_4CH$=N	H	H	H	227–229	..	444
$C_{10}H_{19}NO_3$	Me_3CCH_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
$C_{11}H_{14}NO_3Cl$	*p*-$ClC_6H_4CH_2$	Me	$HOCH_2$	H	119–120	80	351
$C_{11}H_{15}NO_3$	$PhCH_2$	Me	$HOCH_2$	H	92–93	..	351
$C_{11}H_{21}NO_3$	$Me(CH_2)_5$	Me	$HOCH_2$	H	148–150 (0.05)	86	351
	Et_2CHCH_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
$C_{18}H_{16}N_2O_4$	$PhCH_2$	Me	$H_2NCO_2CH_2$	H	132	..	351
$C_{13}H_{15}N_4O_6$	5-Nitro-2-furfurylideneamino	H	H	N-Morpholinomethyl	206	..	32
$C_{13}H_{17}NO_4$	*p*-$MeOC_6H_4CH_2$	Me	$HOCH_2$	H	132–134	90	351
$C_{15}H_{19}N_3O_3$	PhCH=N	H	H	N-Morpholinomethyl	166–167	..	32
$C_{15}H_{21}NO_6$	3,4,5-$(MeO)_3C_6H_2CH_2$	Me	$HOCH_2$	H	136–139, 225–230 (0.02)	..	351

[a] R_5 = 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
$C_5H_9NO_3$	$HOCH_2CH_2$	H	150–155 (0.25)	92	102, 299
$C_{10}H_9NO_2Cl_2$	2,6-$Cl_2C_6H_3CH_2$	H	115.8–118.1	57	306, 518
	3,4-$Cl_2C_6H_3CH_2$	H	68.0–69.6	84	306, 518
	2,4-$Cl_2C_6H_3CH_2$	H	72.2–74.3	79	306
$C_{10}H_{10}NO_2Cl$	*o*-$ClC_6H_4CH_2$	H	70.0–72.1	75	306, 518
	p-$ClC_6H_4CH_2$	H	72.1–73.5	48	306, 518
$C_{10}H_{10}N_2O_4$	*p*-$O_2NC_6H_4CH_2$	H	148.0–150.3	90	306, 518
$C_{10}H_{11}NO_2$	$PhCH_2$	H	78.3–79.2	40	306
$C_{10}H_{11}NO_3$	*p*-$HOC_6H_4CH_2$	H	128.2–129.2	52	306
$C_{10}H_{13}N_2O_2Cl$	*p*-$H_3N^+C_6H_4CH_2Cl^-$	H	190.9–192.1	..	306
$C_{11}H_{11}NO_2Cl_2$	2,4-$Cl_2C_6H_3CH_2$	Me	75.4–77.6	..	518
$C_{11}H_{11}NO_4$	3,4-$CH_2O_2C_6H_3CH_2$	H	59.3–62.2	63	306, 518
$C_{11}H_{13}NO_2$	*p*-$MeC_6H_4CH_2$	H	160–162 (0.03)	92	306
$C_{12}H_{15}NO_3$	*p*-$EtOC_6H_4CH_2$	H	63.4–66.1	68	306, 518
$C_{12}H_{15}NO_4$	3,4-$(MeO)_2C_6H_3CH_2$	H	59.3–62.2	62	306, 518
$C_{12}H_{16}N_4O_6$	5-Nitro-2-furfurylideneamino	N-Morpholinomethyl	205–206 dec	..	312
$C_{13}H_{17}NO_2$	*p*-*i*-$PrC_6H_4CH_2$	H	47.5–49.1	59	306
$C_{14}H_{19}NO_2$	*p*-*n*-$BuC_6H_4CH_2$	H	170–175 (0.04)	87	306, 518

[a] R_2 = R_3 = R_5 = 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
$C_3H_5NO_2$	H	H	...	23	COS	35
	H	H	88–90	90	CO + S	20
$C_5H_9NO_2$	Et	H	...	..	CO + S	20
$C_5H_9NO_4$	$HOCH_2$	$HOCH_2$	106–110	..	CO + S	20

[a] $R_1 = R_4 = R_5 = H$.

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.

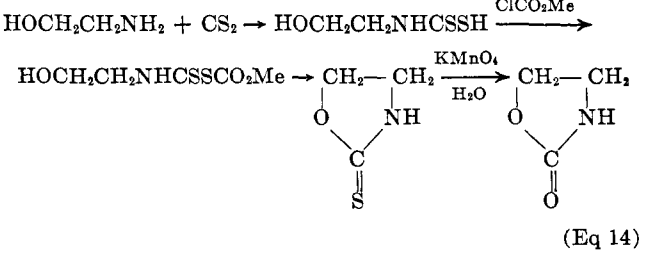
The other group (415) carried out the reaction under nitrogen in the presence of copper and oxygen. They also obtained 3,4-dimethyl-5-phenyl-2-oxazolidone from ephedrine. It has been pointed out that carbon tetrachloride acts as a hydrogen acceptor to form hydrogen chloride and chloroform. No mechanistic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

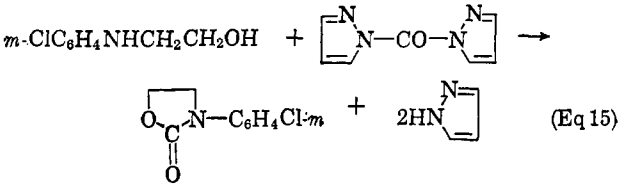
2-Oxazolidone has been prepared (470) by the reaction of β-aminoethanol first with carbon bisulfide followed by methyl chloroformate. This yields the 2-thione which on treatment with aqueous potassium permanganate is converted to the 2-oxazolidone (Eq 14). In the reviewers' opinion the potassium permanganate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



(Eq 14)

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′-carbodiimidazole as the cyclizing reagent (Eq 15) (599).



(Eq 15)

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
$C_3H_5NO_2$	H	...	90	118, 484, 561
$C_5H_9NO_3$	$HOCH_2CH_2$	170 (0.5)	..	484, 561
$C_9H_9NO_2$	Ph	123	..	484, 561

[a] $R_2 = R_3 = R_4 = R_5 = H$.

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
$C_3H_5NO_2$	H	H	90–91 (EtOH)	..	189
$C_5H_8NO_2Cl$	$ClCH_2CH_2$	H	114 (0.3)	95	27, 28
$C_5H_9NO_3$	$HOCH_2CH_2$	H	125–140 (0.1)	..	28
$C_6H_{10}NO_2Cl$	$Cl(CH_2)_3$	H	132–135 (0.5)	82	27
	$ClCH(Me)CH_2$	H	107–108 (0.5)	84	27
$C_7H_{12}NO_2Cl$	$Cl(CH_2)_3$	Me	112–114 (0.1)	50	27

[a] $R_2 = R_3 = R_5 = H$.

TABLE XI

2-OXAZOLIDONES PREPARED FROM β-HALO ALCOHOLS AND UREA

Empirical formula[a]	R_4	Mp, °C	% yield	Ref
$C_{11}H_{13}NO_3$	o-$MeC_6H_4OCH_2$	128–129 (EtOAc)	..	44
$C_{11}H_{13}NO_4$	o-$MeOC_6H_4OCH_2$	140.5–142 (EtOH)	..	323
$C_{12}H_{15}NO_5$	3,5-$(MeO)_2C_6H_3OCH_2$	124–125	..	427
$C_{13}H_{17}NO_3$	2,3,5-$Me_3C_6H_2OCH_2$	125–126	60	427
	3,4,5-$Me_3C_6H_2OCH_2$	129–132	..	427

[a] $R_1 = R_2 = R_3 = R_5 = H$.

TABLE XII

2-OXAZOLIDONES PREPARED FROM β-HALO ALCOHOLS AND URETHANS

Empirical formula[a]	R_1	R_2	R_4	Mp, °C	% yield	Ref
$C_{10}H_{10}N_2O_2$	PhCH= N	H	H	142–143 (EtOH)	78	481
$C_{10}H_{11}N_3O_5$	5-Nitro-2-furfuryli-deneamino	Me	Me	140.5–143.0	66	481
$C_{15}H_{29}NO_2$	$C_{12}H_{25}$	H	H	62	53	530

[a] $R_3 = R_5 = H$.

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*

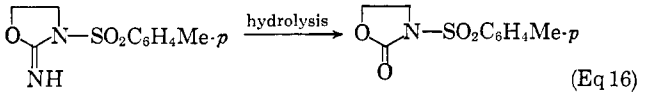
Many years ago, Fromm and Honold (182) obtained a derivative of 2-oxazolidone by the sequence shown in Eq 16.

$$ClCH_2CH_2OH + Na_2NCN \rightarrow$$

$$NaCl + NC{-}N(Na)CH_2CH_2OH \xrightarrow{H^+}$$

$$NC{-}NHCH_2CH_2OH \xrightarrow{p\text{-}MeC_6H_4SO_2Cl}$$

$$p\text{-}MeC_6H_4SO_2N(CN)CH_2CH_2OH \rightarrow$$

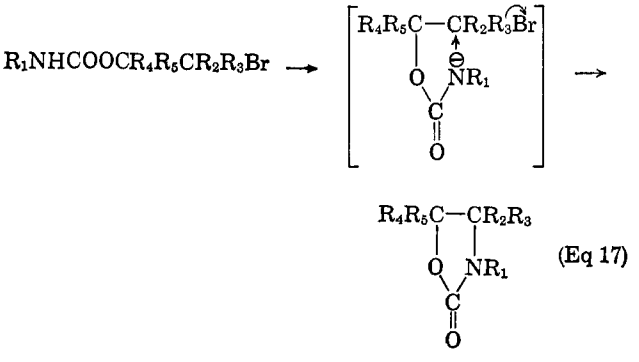


(Eq 16)

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).

$$R_1NHCOOEt + HOCR_4R_5CR_2R_3Br \xrightarrow{base}$$



(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
$C_3H_5NO_2$	H	H	79–80 (dioxane–Et_2O)	93	184
$C_4H_7NO_2$	Me	H	...	79	184
$C_8H_{13}NO_2$	$-(CH_2)_5-$		101–102 (dioxane)	44	184
$C_9H_{10}NO_2$	Ph	H	...	..	184
$C_{10}H_{10}NO_3Cl$	o-$ClC_6H_4OCH_2$	H	151 (EtOAc)	..	44
$C_{11}H_{13}NO_3$	o-$MeC_6H_4OCH_2$	H	128–129 (EtOAc)	..	44

[a] $R_1 = R_2 = R_3 = H$.

TABLE XIV

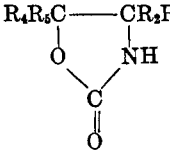
2-OXAZOLIDONES PREPARED FROM β-HALOETHANOLS AND PHOSGENE PLUS PRIMARY AMINES

Empirical formula[a]	R_1	Bp (mm) or mp, °C	% yield	Ref
$C_3H_4NO_2Cl$	Cl	122	82	66
$C_7H_{13}NO_2$	n-C_4H_9	132 (3)	70	66
$C_8H_{15}NO_2$	n-C_5H_{11}	145 (4)	68	66
$C_9H_8NO_2Cl$	o-ClC_6H_4	185–188 (3), 192–194 (7)	82	5, 66
	m-ClC_6H_4	53–54	73	66
	p-ClC_6H_4	121–122, 118.5–119.0 (EtOH)	80	5, 66
$C_9H_9NO_2$	Ph	...	..	4, 379
$C_9H_{17}NO_2$	n-C_6H_{13}	176 (1)	82	66
$C_{10}H_{11}NO_2$	o-MeC_6H_4	180–185 (3)	..	5
	p-MeC_6H_4	91 (EtOH)	...	5
$C_{11}H_{13}NO_3$	p-$EtOC_6H_4$	96 (EtOH–Et_2O)	...	4, 5
$C_{13}H_{11}NO_2$	α-Naphthyl	130	78	66

[a] $R_2 = R_3 = R_4 = R_5 = H$.

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

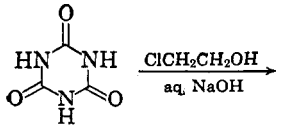
$$HOCR_4R_5CR_2R_3Cl + NCO^- \rightarrow [HOCR_4R_5CR_2R_3NCO] \rightarrow$$

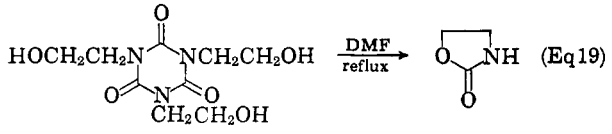


(Eq 18)

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).

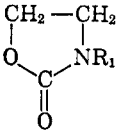




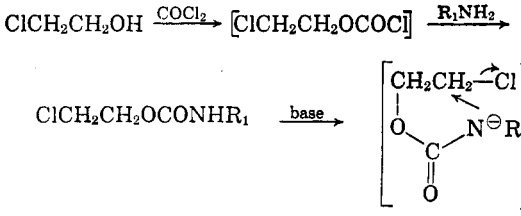
(Eq 19)

6. *Use of Phosgene plus Amines (Table XIV)*

Another early method is the reaction of phosgene and aniline with β-chloroethanol to produce β-chloroethyl N-phenylcarbamate, which is cyclized by boiling in potassium hydroxide solution (379) (Eq 20).



(Eq 20)

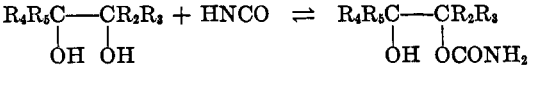


F. FROM 1,2-GLYCOLS

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).

$$2H_2NCONH_2 \overset{\Delta}{\rightleftharpoons} 2HNCO + 2NH_3 \quad \text{(Eq 21a)}$$



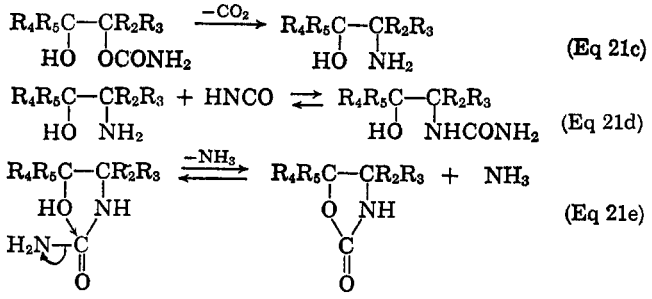
(Eq 21b)

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
$C_3H_5NO_2$	H	H	91, 87–89 ($CHCl_3$)	..	260, 406
$C_{10}H_8NO_3Cl_3$	H	2,4,6-$Cl_3C_6H_2OCH_2$	...	..	319
$C_{10}H_9NO_3Cl_2$	H	2,4-$Cl_2C_6H_3OCH_2$	128–130 (EtOAc)	42	319, 325
$C_{10}H_{10}NO_3Cl$	H	*o*-$ClC_6H_4OCH_2$	147–148 (EtOAc)	48	325
	H	*m*-$ClC_6H_4OCH_2$	96.5–97 (EtOAc)	76	325
	H	*p*-$ClC_6H_4OCH_2$	143.5–146 (EtOAc)	59	325
$C_{10}H_{10}NO_3Br$	H	*p*-$BrC_6H_4OCH_2$	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	*o*-$HOC_6H_4OCH_2$	84–86 (EtOAc)	20	325
$C_{11}H_{12}NO_3F$	H	2-Me-4-$FC_6H_3OCH_2$	...	..	319
	H	3-Me-4-$FC_6H_3OCH_2$	...	..	320
$C_{11}H_{12}NO_3Cl$	H	2-Me-5-$ClC_6H_3OCH_2$	104–104.5 (EtOAc)	57	319, 325
	H	2-Me-3-$ClC_6H_3OCH_2$	124.0–125.5 (EtOAc)	35	325
	H	3-Me-4-$ClC_6H_3OCH_2$	135–137 (EtOAc)	36	325
$C_{11}H_{12}NO_3Br$	H	2-Me-4-$BrC_6H_3OCH_2$	...	..	319
	H	3-Me-4-$BrC_6H_3OCH_2$	...	..	320
$C_{11}H_{13}NO_3$	H	*o*-$MeC_6H_4OCH_2$	127–129, 124.5–125.5 (MeOH)	94	44, 325
	H	*m*-$MeC_6H_4OCH_2$	102–103, 225–240 (0.35)	54	325
	H	*p*-$MeC_6H_4OCH_2$	131–131.5 (EtOAc)	58	325
$C_{11}H_{12}NO_3Cl$	Me	*o*-$ClC_6H_4OCH_2$	79–81	..	12
	Me	*m*-$ClC_6H_4OCH_2$	...	..	12
$C_{11}H_{13}NO_4$	H	*o*-$MeOC_6H_4OCH_2$	140.5–142.0 (EtOH); 141–143 (H_2O); 143–145 (95% EtOH)	67	12, 321, 323, 325
	H	*m*-$MeOC_6H_4OCH_2$	121–123, 125.0–126.5 (EtOAc)	48	12, 325
	H	*p*-$MeOC_6H_4OCH_2$	135–136 (EtOAc)	50	325
$C_{12}H_{14}NO_3Cl$	Me	3-Me,4-$ClC_6H_3OCH_2$	...	..	320
$C_{12}H_{15}NO_3$	Me	*m*-$MeC_6H_4OCH_2$	73.5	..	12
	H	3,4-$Me_2C_6H_3OCH_2$	116–117 (EtOAc)	37	325
	H	3,5-$Me_2C_6H_3OCH_2$	121.5–123.0 (EtOAc), 220–225 (1.5)	79	325, 437
	H	2,6-$Me_2C_6H_3OCH_2$	104–105 (EtOAc), 220–235 (0.35)	74	319, 325
$C_{12}H_{15}NO_4$	Me	*o*-$MeOC_6H_4OCH_2$	72.5–75.0 (C_6H_6–Et_2O)	..	12
	Me	*p*-$MeOC_6H_4OCH_2$	...	..	12
	H	*o*-$EtOC_6H_4OCH_2$	98–100, 105–106	42	12, 260
$C_{12}H_{15}NO_5$	H	2,6-$(MeO)_2C_6H_3OCH_2$	104–105, 117.5–118.5 (EtOAc)	52	319, 324, 325
	H	3,5-$(MeO)_2C_6H_3OCH_2$	124–125 (EtOAc), 245–257 (0.15)	75	325, 437
$C_{13}H_{16}NO_3Cl$	H	2-Pr-6-$ClC_6H_3OCH_2$	...	..	319
	Et	3-Me-4-$ClC_6H_3OCH_2$	95.5–96.0 (*i*-Pr_2O)	..	320
$C_{13}H_{16}NO_3Br$	H	3-Pr-4-$BrC_6H_3OCH_2$	...	..	320
$C_{13}H_{16}NO_4Cl$	H	2-PrO-6-$ClC_6H_3OCH_2$	...	..	319
$C_{13}H_{17}NO_3$	H	3,4,5-$Me_3C_6H_2OCH_2$	129–132	..	437
	H	2,3,5-$Me_3C_6H_2OCH_2$	125–126 (EtOAc)	60	325, 437
$C_{13}H_{17}NO_4$	Et	*o*-$MeOC_6H_4OCH_2$	175–178 (0.1)	..	12
	H	2-MeO-4-$BrC_6H_3OCH_2$	106–108	63	260
$C_{13}H_{17}NO_6$	H	3,4,5-$(MeO)_3C_6H_2OCH_2$	129–132 (EtOAc), 265–280 (0.15)	60	325
$C_{14}H_{17}NO_4$	H	2-MeO-6-$(CH_2{=}CHCH_2)C_6H_3OCH_2$	...	..	319
$C_{14}H_{18}NO_3Cl$	Pr	3-Me-4-$ClC_6H_3OCH_2$	...	..	320
$C_{14}H_{19}NO_3$	H	2,6-$Et_2C_6H_3OCH_2$	...	..	319
$C_{14}H_{19}NO_4$	H	*p*-$BuOC_6H_4OCH_2$	139.5–141.5 (EtOAc)	45	325
	H	*o*-$BuOC_6H_4OCH_2$	62–63 (EtOAc), 235–255 (0.1)	71	325
$C_{16}H_{23}NO_5$	H	2,6-$(PrO)_2C_6H_3OCH_2$	...	...	319

[a] $R_2 = R_3 = R_5 = H$.



(Eq 21c)

(Eq 21d)

(Eq 21e)

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
$C_{11}H_{13}NO_3$	o-$MeC_6H_4OCH_2$	130–131 (EtOH)	..	59, 105, 300
$C_{11}H_{13}NO_4$	o-$MeOC_6H_4OCH_2$	145–146 (EtOH)	..	59, 300
$C_{13}H_{17}NO_4$	2-Me-4-$EtOC_6H_3OCH_2$	...	..	108
$C_{14}H_{17}NO_4$	2-MeO-4-(MeCH=CH)$C_6H_3OCH_2$	116–117	..	108
	2-MeO-4-(CH_2=$CHCH_2$)$C_6H_3OCH_2$	109–110	..	108
$C_{14}H_{19}NO_4$	2-MeO-4-$PrC_6H_3OCH_2$	103–104	..	108
$C_{16}H_{15}NO_3$	o-$PhC_6H_4OCH_2$	99–100, 205–230 (0.1)	48	108
	p-$PhC_6H_4OCH_2$	195–196	..	108

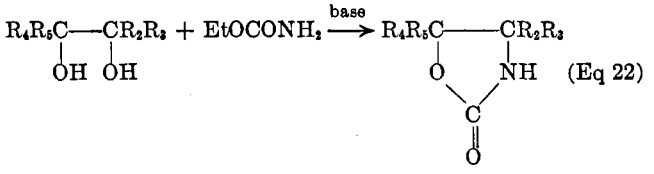
[a] $R_1 = R_2 = R_3 = R_5 = H$.

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
$C_3H_5NO_2$	H	H	H	85–87 (MeOH), 89–90, 130–140 (1–2)	90	111, 179, 311
$C_4H_7NO_2$	H	H	Me	111–113 (1), 113–118 (3)	..	111, 311
$C_5H_7NO_2$	H	H	CH_2=CH	41–44 (Et_2O), 125–130 (0.1)	..	310
$C_5H_9NO_3$	$HOCH_2CH_2$	H	H	145–165 (1)	...	177
$C_6H_{11}NO_3$	$HOCH_2CH_2$	H	Me	123–128 (0.1)	..	177
$C_9H_8NO_2Cl$	p-ClC_6H_4	H	H	119–120	..	134
$C_9H_9NO_2$	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	$-(CH_2)_4-$		168–173 (0.3)	...	134
$C_{14}H_{17}NO_2$	Ph	(4-Pentenyl)[b]	(4-Pentenyl)[b]	161–163 (0.15)	...	134

[a] $R_3 = R_5 = H$. [b] Position of substituent in doubt.



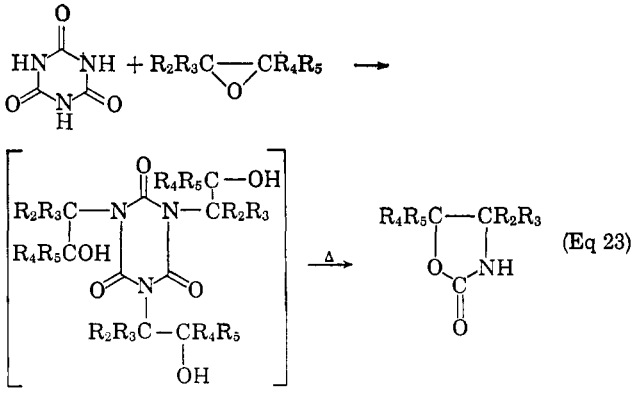
G. FROM 1,2-DIHALIDES

A single patent (533) reports the preparation of 2-oxazolidone, mp 88° [EtOH or $(CH_2Cl)_2$] 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 $R_1 = H$, but when R_1 is a substituent group a different mechanism must apply (see section IIH2 below for the reaction of epoxides with organic isocyanates).

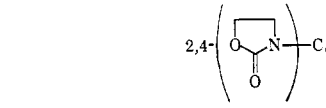
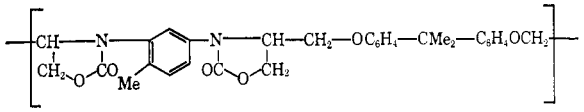


2. Use of Organic Isocyanates (Table XVIII) and Inorganic Cyanates

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

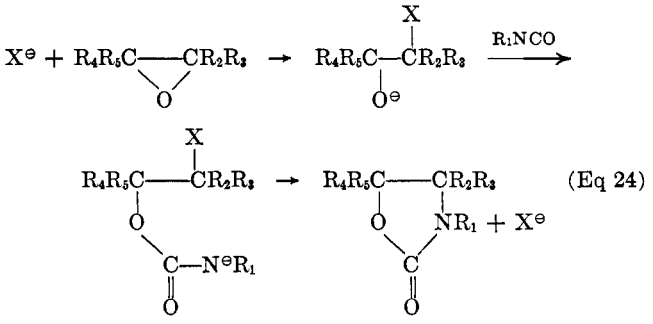
2-OXAZOLIDONES PREPARED FROM EPOXIDES AND ORGANIC ISOCYANATES

Empirical formula[a]	R_1	R_2	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_5H_9NO_2$	Et	H	H	129–130 (10), 65–68 (0.15)	26	269, 398, 491
$C_9H_9NO_2$	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
$C_{13}H_{15}NO_3$	Ph	H	CH_2=$CHCH_2OCH_2$	176 (0.06)	76	214
$C_{15}H_{19}NO_2$	Cyclohexyl	H	Ph	95–96 (pet. ether)	90	214
$C_{16}H_{15}NO_2$	$PhCH_2$	H	Ph	210–220 (0.4)	39	214
$C_{16}H_{15}NO_3$	Ph	H	$PhOCH_2$	134.5–136.5, 137–138 (C_6H_6), 233–234 (0.5)	88	215, 479, 491, 592
$C_{16}H_{21}NO_3$	Cyclohexyl	H	$PhOCH_2$	147.0–147.5 (pet. ether), 200–202 (0.2)	96	214
$C_{19}H_{29}NO_2$	Ph	H	n-$C_{10}H_{21}$	68.5–69.7 (pet. ether)	25	269
$C_{22}H_{34}NO_3$	n-$C_{12}H_{25}$	H	$PhOCH_2$	62 (EtOH), 231–232 (0.2)	64	214
				137.5 (EtOH, then C_6H_6)	53	491
				175–185	91	452

[a] $R_3 = R_5 = H$. [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.



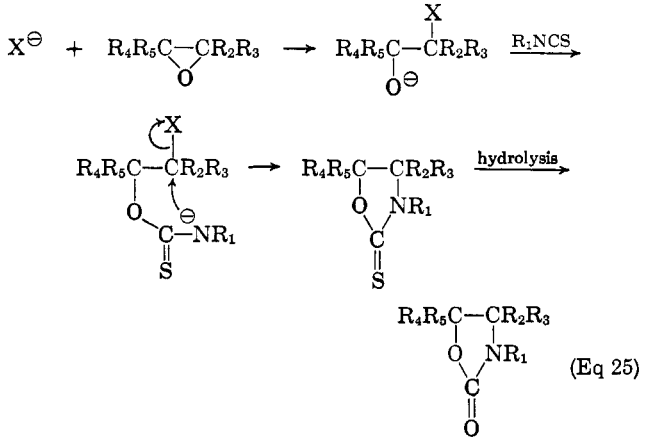
(Eq 24)

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.

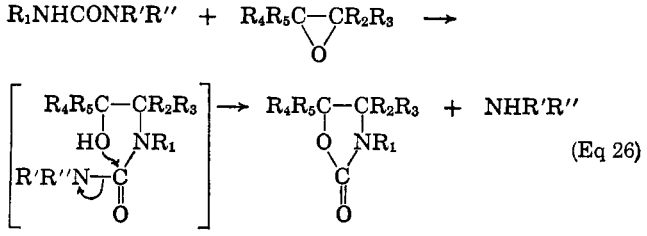
A proposed mechanism is given in Eq 25. It suggests the formation of an intermediate 2-oxazolidinethione which is hydrolyzed to the product.



(Eq 25)

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



(Eq 26)

TABLE XIX

2-OXAZOLIDONES PREPARED FROM EPOXIDES AND ISOTHIOCYANATES

Empirical formula[a]	R_1	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_9H_9NO_2$	Ph	H	121 (CH_2Cl_2–pet. ether)	60	164, 169
$C_{10}H_{10}NO_2Cl$	Ph	$ClCH_2$	103	85	164
$C_{10}H_{11}NO_2$	Ph	Me	81.5	45	164
$C_{16}H_{15}NO_3$	Ph	$PhOCH_2$	137–138 (CH_2Cl_2–pet. ether)	25	169

[a] $R_2 = R_3 = R_5 = H$.

TABLE XX

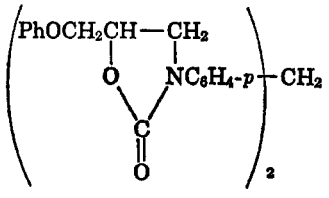
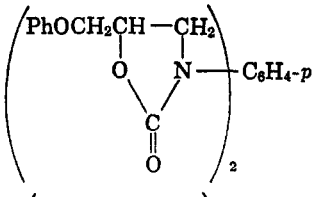
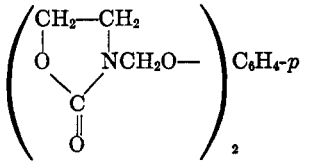
2-OXAZOLIDONES PREPARED FROM EPOXIDES AND UREA

Empirical formula[a]	R_1	R_4	Bp (mm) or mp, °C	Ref
$C_3H_5NO_2$	H	H	89 (EtOH)	394
$C_{10}H_{11}NO_3$	H	$PhOCH_2$	124, 225–227 (5)	393
$C_{11}H_{13}NO_3$	H	o-$MeC_6H_4OCH_2$	125–127 ($CHCl_3$–ligroin)	44
$C_{11}H_{13}NO_4$	H	o-$MeOC_6H_4OCH_2$	140.5–142.0 (EtOH)	323
$C_{16}H_{15}NO_3$	Ph	$PhOCH_2$	...	263

[a] $R_2 = R_3 = R_5 = H$.

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
$C_8H_7N_2O_5$	5-Nitro-2-furfurylideneamino	H	...	...	391
$C_{10}H_{10}NO_3Cl$	H	o-$ClC_6H_4OCH_2$	146.9–151.0 (EtOAc)	...	328
$C_{11}H_{13}NO_3$	H	o-$MeC_6H_4OCH_2$	128–129 (EtOH)	...	44
$C_{11}H_{13}NO_4$	H	o-$MeOC_6H_4OCH_2$	140.5–142.0 (EtOH) 141.4–141.9 (H_2O)	...	323, 328
$C_{12}H_{15}NO_3$	H	3,5-$Me_2C_6H_3OCH_2$	...	...	328
$C_{14}H_{15}N_2O_3$	2-Pyridyl	$PhOCH_2$	115–116 (EtOH)	...	263
$C_{16}H_{14}NO_3Cl$	p-ClC_6H_4	$PhOCH_2$	158–162 (Me_2CO)	...	263
$C_{16}H_{14}N_2O_5$	p-$O_2NC_6H_4$	$PhOCH_2$	162–163 (Me_2CO)	...	263, 264
$C_{16}H_{15}NO_3$	Ph	$PhOCH_2$	139–140 (Me_2CO)	100	263, 264
$C_{17}H_{17}NO_3$	p-MeC_6H_4	$PhOCH_2$	149–151 (Me_2CO)	...	263
$C_{18}H_{19}NO_4$	p-$EtOC_6H_4$	$PhOCH_2$	131–133 (Me_2CO)	...	263
Structure					
					264
			185–187		264
			206–210		264

[a] $R_2 = R_3 = R_5 = H$.

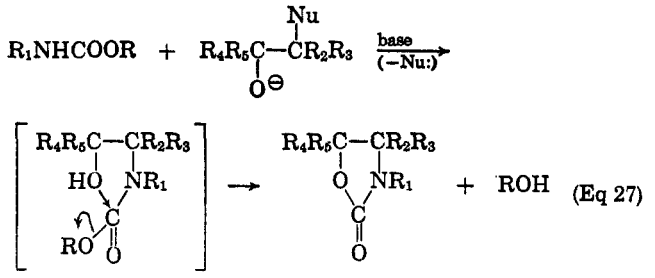
on this reaction. The reaction is carried out without solvent or catalyst at high temperatures.

5. *Use of Urethans (Table XXI)*

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

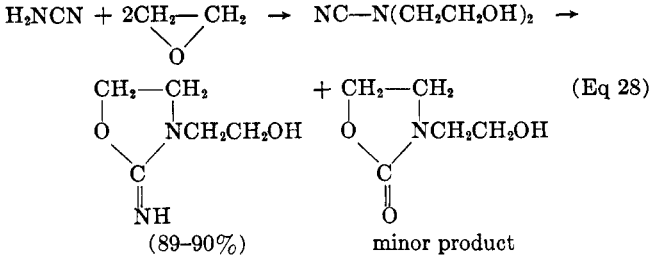
ethyl)urethan which cyclizes with loss of alcohol (Eq 27).



(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.

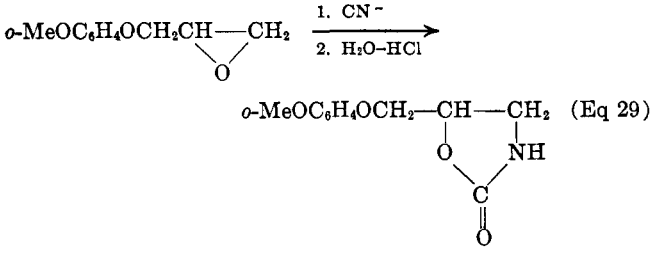


(Eq 28)

(89–90%) minor product

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).



(Eq 29)

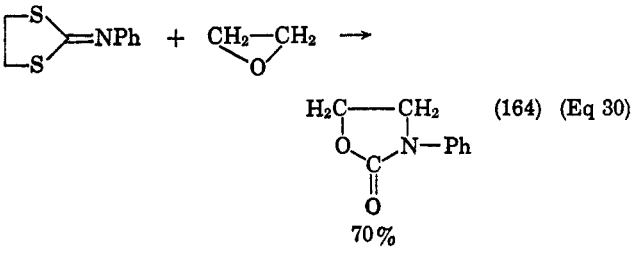
8. *Use of Dithiolanes and Oxathiolanes (Table XXII)*

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

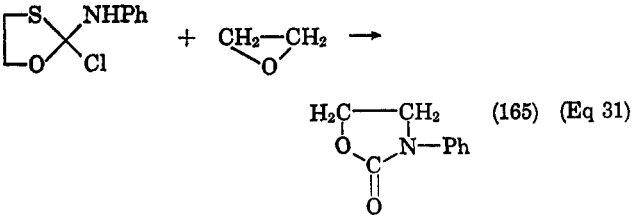
2-OXAZOLIDONES PREPARED ACCORDING TO EQ 32

Empirical formula	R	Mp, °C	% yield	Ref
$C_9H_9NO_2$	H	120	63	165
$C_{10}H_{10}NO_2Cl$	$ClCH_2$	103	51	165
$C_{10}H_{11}NO_2$	Me	81.5	51	165

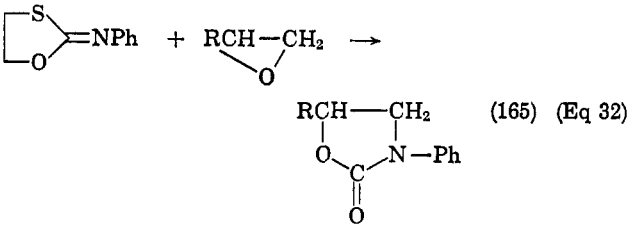


(164) (Eq 30)

70%



(165) (Eq 31)



(165) (Eq 32)

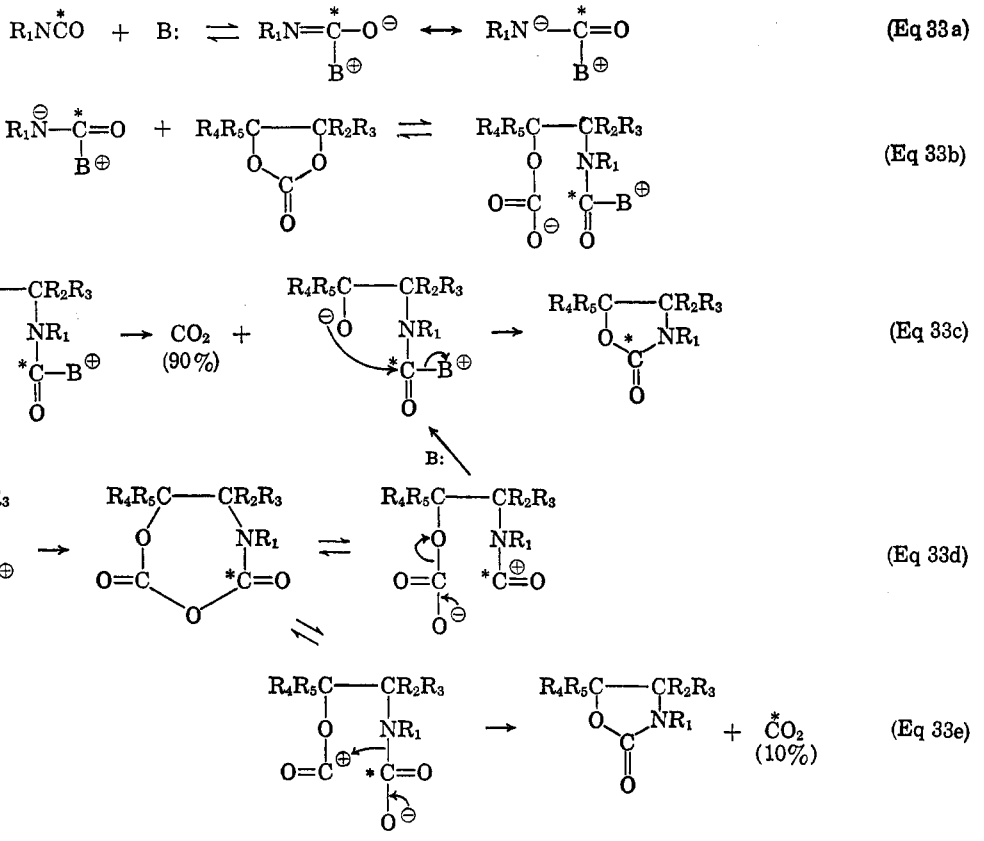
I. FROM CYCLIC CARBONATES (2-DIOXOLANONES)

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.



(Eq 33a)

(Eq 33b)

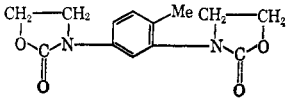
(Eq 33c)

(Eq 33d)

(Eq 33e)

TABLE XXIII

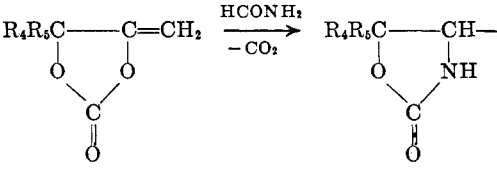
2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES AND ISOCYANATES

Empirical formula[a]	R_1	R_2	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_7H_{13}NO_2$	n-C_4H_9	H	H	122–124 (18)	91	216
$C_9H_8NO_2Cl$	p-ClC_6H_4	H	H	116–117	70	548, 550
$C_9H_9NO_2$	Ph	H	H	117–119 (EtOH), 121–122, 196 (2)	92	214–216, 226, 548–550
$C_9H_{15}NO_2$	Cyclohexyl	H	H	33–33.4	95	214, 215
$C_{14}H_{11}NO_2$	p-MeC_6H_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
$C_{11}H_{13}NO_3$	p-$EtOC_6H_4$	H	H	95–96	78	548
$C_{12}H_{13}NO_4$	p-$EtOCOC_6H_4$	H	H	109.5	98	214, 215
$C_{13}H_{15}NO_4$	p-$EtOCOC_6H_4$	H	Me	97–98	91	214, 215
$C_{15}H_{29}NO_2$	n-$C_{12}H_{25}$	H	H	167–168 (0.25)	54	214
$C_{16}H_{31}NO_2$	n-$C_{12}H_{25}$	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] $R_3 = R_5 = H$.

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.



(Eq 34)

TABLE XXIV

2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES AND FORMAMIDE

Empirical formula[a]	R_4	R_5	Bp (mm) or mp, °C	Ref
$C_6H_{11}NO_2$	Me	Me	60–62 (Et_2O–pet. ether), 114–119 (0.1)	456
$C_7H_{13}NO_2$	Me	Et	129–130 (0.3)	456
$C_9H_{15}NO_2$	$-(CH_2)_5-$		110–111 (EtOAc), 155–167 (0.1)	456
$C_9H_{19}NO_2$	Me	*i*-Bu	39–41 (pet. ether), 139–146 (0.1)	456
$C_{11}H_{19}NO_2$	$-(CH_2)_7-$		108 (0.25)	456

[a] $R_1 = R_2 = H$; $R_3 = CH_3$.

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).

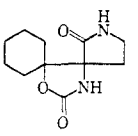
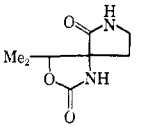
J. FROM ACETYLENIC COMPOUNDS

1. *Acetylenic Alcohols plus Isocyanates (Table XXVI)*

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

TABLE XXV

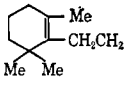
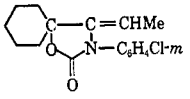
2-OXAZOLIDONES PREPARED FROM CYCLIC CARBONATES AND AMMONIUM CARBONATE AND POTASSIUM CYANIDE

Empirical formula[a]	R_2	R_3	R_4	R_5	Mp, °C	Ref
$C_7H_{10}N_2O_2$	NC	Me	Me	Me	106–107 (EtOAc–pet. ether)	458
$C_7H_{10}N_2O_3$	NC	$HOCH_2$	Me	Me	110–112	458
$C_7H_{12}N_2O_3$	H_2NCO	Me	Me	Me	207–209 (H_2O)	457
$C_8H_{10}N_2O_3$	NC	Me	Me	$OHCCH_2$	...	458
$C_8H_{10}N_2O_4$	NC	Me	Me	MeOCO	135–137	458
$C_8H_{12}N_2O_2$	NC	Me	Me	Et	88–89	458
$C_8H_{12}N_2O_3$	NC	Me	Me	$MeOCH_2$	...	458
	NC	$MeOCH_2$	Me	Me	135–136	458
$C_8H_{14}N_2O_3$	H_2NCO	Me	Me	Et	224–226 (EtOH)	457
$C_8H_{14}N_2O_4$	H_2NCO	Me	Me	$MeOCH_2$	205–206 (MeOH)	457
$C_9H_{16}N_2O_3$	H_2NCO	Me	Me	*i*-Pr	192–194 (EtOH)	457
$C_9H_{16}N_2O_4$	H_2NCO	Me	Me	$Me_2C(OH)$	189–191 (aq HOAc)	457
$C_{10}H_{14}N_2O_2$	NC	Me		$-(CH_2)_5-$	133–134	458
$C_{10}H_{14}N_2O_3$	NC	$HOCH_2$		$-(CH_2)_5-$	240–249	458
$C_{10}H_{16}N_2O_2$	NC	Me	Me	*i*-Bu	80–83	458
$C_{10}H_{16}N_2O_3$	H_2NCO	Me		$-(CH_2)_5-$	253–254 (HOAc)	457
$C_{11}H_{12}N_3O_2$	NC	Me	Me	α-Pyridyl	143–144.5	458
$C_{11}H_{14}N_2O_3$	NC	$Me_2C(OH)C{\equiv}C$	Me	Me	210–211	458
$C_{11}H_{16}N_2O_3$	NC	$MeOCH_2$		$-(CH_2)_5-$	152–153	458
$C_{11}H_{19}N_3O_2$	NC	Et_2NCH_2	Me	Me	...	458
$C_{12}H_{12}N_2O_2$	NC	Me	Me	Ph	139.5–140.5	458
$C_{12}H_{14}N_3O_3$	H_2NCO	Me	Me	Ph	217–219 (malonic ester)	457
$C_{12}H_{18}N_2O_3$	NC	Me		$-(CH_2)_7-$	106.5–107.5	458
	NC	Me	Me	3-Methyl-3-pentenyl	82–83	458
$C_{12}H_{18}N_2O_4$	H_2NCO	$Me_2C(OH)C{\equiv}CCH_2$	Me	Me	211–213 (DMF–H_2O)	458
$C_{13}H_{14}N_2O_2$	NC	$PhCH_2$	Me	Me	149	457
$C_{13}H_{16}N_2O_3$	H_2NCO	$PhCH_2$	Me	Me	226–227 (THF–pet. ether)	457
$C_{13}H_{18}N_2O_2$	NC	$CH_2{=}CH(CH_2)_2$		$-(CH_2)_5-$	133.5–135.5	458
$C_{13}H_{23}N_3O_2$	NC	Me	Me	$Et_2N(CH_2)_3$	Oil	458
$C_{13}H_{23}N_3O_3$	NC	β-(N-Morpholino)ethyl		$-(CH_2)_5-$	133–134	458
$C_{13}H_{25}N_3O_3$	H_2NCO	Me	Me	$Et_2N(CH_2)_3$	164–165 (THF–pet. ether)	457
$C_{16}H_{26}N_2O_2$	NC	Me		$-(CH_2)_{11}-$	156–158	458
$C_{16}H_{28}N_2O_3$	H_2NCO	Me		$-(CH_2)_{11}-$	258–260 (N-methylpyrrolidone)	457
$C_{17}H_{26}N_2O_2$	NC	Me	Me	4,8-Dimethyl-3,7-nonadienyl	...	458
$C_{22}H_{40}N_2O_2$	NC	Me	Me	4,8,12-Trimethyltridecyl	...	458
					283 dec (malonic ester–HOAc)	457
					281–285 dec (HOAc–MeOH)	457

[a] $R_1 = H$.

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
$C_8H_{13}NO_2$	Et	Me	Me	72–74 (0.3–0.6)	70	471
$C_9H_{15}NO_2$	Et	Me	Et	87–91 (1.2–1.5)	60	471
$C_{10}H_7NO_2Cl_2$	3,4-$Cl_2C_6H_3$	H	H	152–153	93	504
$C_{10}H_9NO_2$	Ph	H	H	94–97 ($CHCl_3$–isooctane); 97.2–97.7 (MeOH), 97.5–98.0	96	83, 471, 503, 504
$C_{12}H_{11}NO_2Cl_2$	3,4-$Cl_2C_6H_3$	Me	Me	134.2–135.1, 140.2–140.8	63	83, 504
$C_{12}H_{12}NO_2Cl$	*m*-ClC_6H_4	Me	Me	102.0–102.5	..	83
$C_{12}H_{13}NO_2Cl$	Ph	Me	Me	130–133 (EtOH), 131.5–132.0	90	83, 471
$C_{13}H_{13}NO_2Cl$	3,4-$Cl_2C_6H_3$	Et	Me	87–89 (pet. ether), 88.1–88.9	90	471, 504
	2,5-$Cl_2C_6H_3$	Me	Et	134–135 (1,2-dimethoxyethane)	50	471
	3,4-$Cl_2C_6H_3$	Me	Et	88.6–88.8	..	83
$C_{13}H_{14}NO_2Cl$	*p*-ClC_6H_4	Me	Et	112–119 (Et_2O)	60	471
$C_{15}H_{15}NO_2Cl_2$	3,4-$Cl_2C_6H_3$	$-(CH_2)_5-$		161.5–162.1	67	504
$C_{15}H_{16}NO_2Cl$	*m*-ClC_6H_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] R_2R_3 = methylene.

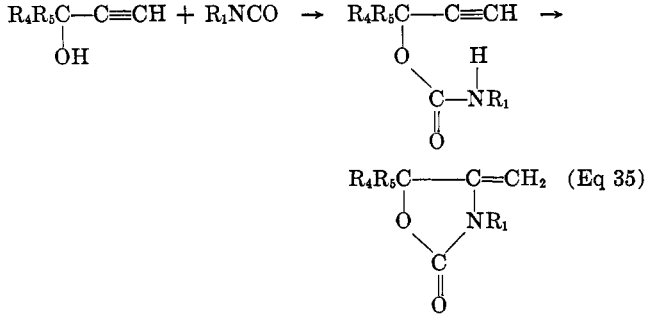
TABLE XXVII

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

Empirical formula[a]	R_1	R_3	Mp, °C	% yield	Ref
$C_{10}H_9NO_2Cl_2$	3,4-$Cl_2C_6H_3$	Me	88.7–89.5 (MeOH)	73	504
$C_{10}H_{11}NO_2$	Ph	Me	49–50° (Et_2O)	66	504

[a] R_3 = R_4 = R_5 = 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.

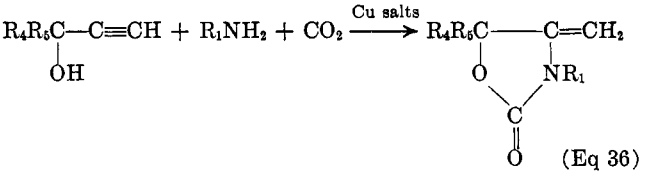


(Eq 35)

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)*

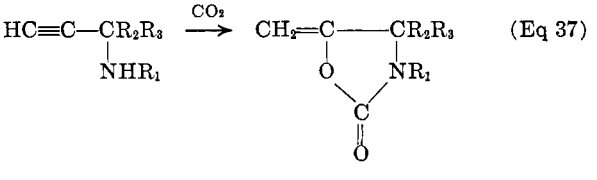
5,5-Disubstituted 4-methylene-2-oxazolidones are obtained by the reaction of acetylenic alcohols with amines and carbon dioxide at elevated temperatures and pressures in the presence of catalytic amounts of copper salts (133) (Eq 36).



(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.

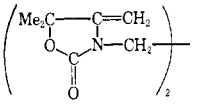


(Eq 37)

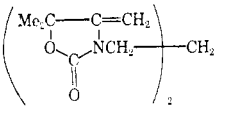
TABLE XXVIII

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_5	Bp (mm) or mp, °C
$C_7H_{11}NO_2$	Me	Me	Me	94 (15)
$C_8H_{13}NO_3$	$HOCH_2CH_2$	Me	Me	71–73 (EtOAc), 128–130 (0.6)
$C_9H_{15}NO_4$	*i*-Pr	Me	Me	66–69, 110–114 (21)
$C_{10}H_{15}NO_2$	Me	$-(CH_2)_5-$		58–60, 118–120 (1)
$C_{10}H_{17}NO_2$	*n*-Bu	Me	Me	...
$C_{11}H_7NO_2$	$CH_2{=}C(Me)CH(Me)$	Me	Me	88–90 (0.3)
$C_{11}H_{19}NO_2$	*n*-Bu	Me	Et	89–93 (0.5)
$C_{17}H_{19}NO_2$	*i*-Pr	$-(CH_2)_5-$		89, 138–141 (1)
	Cyclohexyl	Me	Me	68, 140 (0.6)
$C_{13}H_{15}NO_2$	$PhCH_2$	Me	Me	32–34, 118–121 (0.9)
$C_{13}H_{11}NO_2$	*n*-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] R_2R_3 = methylene.

TABLE XXIX

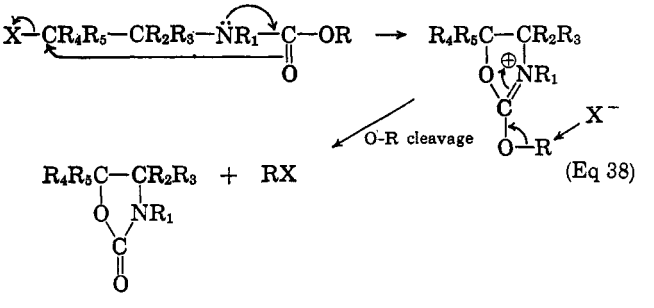
4,4-DISUBSTITUTED 5-METHYLENE-2-OXAZOLIDONES PREPARED FROM ACETYLENIC AMINES AND CARBON DIOXIDE (131)

Empirical formula[a]	R_1	R_2	R_3	Bp (mm) or mp, °C
$C_8H_{13}NO_2$	*i*-Pr	Me	H	67 (0.3)
$C_9H_{13}NO_2$	H	$-(CH_2)_5-$		112
$C_9H_{15}NO_2$	*i*-Pr	Me	Me	125–127 (EtOAc)
$C_{10}H_{17}NO_2$	*n*-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)
$C_{13}H_{21}NO_2$	*n*-Bu	$-(CH_2)_5-$		130 (0.15)

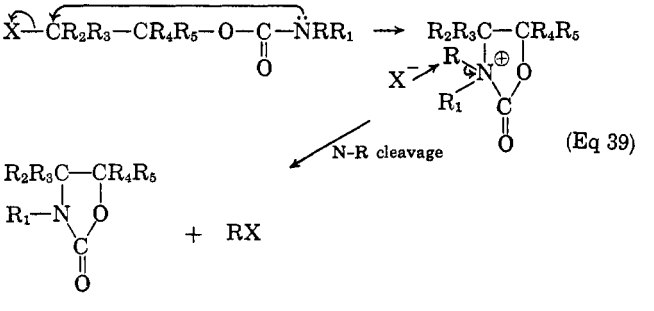
[a] R_4R_5 = methylene.

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 R_1 = H), and alkaline catalysts are usually present. A mechanism involving intermediate carbonium ions



(Eq 38)



(Eq 39)

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

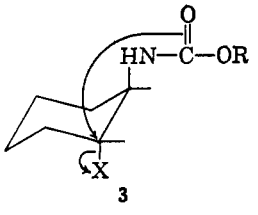
2-OXAZOLIDONES PREPARED BY PYROLYSIS OF β-SUBSTITUTED URETHANS

Empirical Formula[a]	R_1	R_2	R_3	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	H	H	...	50	543
$C_4H_6NO_2Cl$	H	H	H	$ClCH_2$	105–106 (H_2O)	80	286
$C_4H_7NO_2$	H	H	H	Me	109–111 (2), 136–137 (5)	90	286, 368, 543
	H	Me	H	H	155–160 (11)	Poor	368
$C_5H_8NO_2Br$	H	H	H	$BrCH_2CH_2$	107 (C_6H_6)	70	286
	Me	H	H	$BrCH_2$	180–190	...	13
$C_5H_9NO_2$	H	H	H	Et	109 (0.15)	90	543
	H	Et	H	H	...	Poor	368
	H	Me	Me	H	152–154	...	286
$C_6H_{10}NO_2Cl$	Et	H	H	$ClCH_2$	...	...	13
$C_7H_{11}NO_2$	H	H	$-(CH_2)_4-$		*trans*, 100–102 ($CHCl_3$–pet. ether);	...	358
					cis, 55–56 (Et_2O–pet. ether)	...	230, 358
$C_8H_{13}NO_2$	Me	H	$-(CH_2)_4-$		*trans*, 51–52 (EtOAc–pet. ether);	...	358
					cis, 110–115 (0.02)	...	358
$C_9H_9NO_2$	Ph	H	H	H	...	95	42, 286
	H	H	H	Ph	90–91 ($CHCl_3$–C_6H_6)	45	543
	H	Ph	H	H	136	...	230

Name							
Cholestano[3β,2β-*b*]-2-oxazolidone					227		230
cis-Tetralino[2,1-*b*]-2-oxazolidone					141		230
cis-Indano[2,1-*b*]-2-oxazolidone					160		230

[a] R_5 = 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.

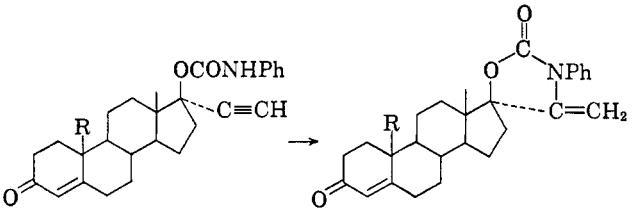


3

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.



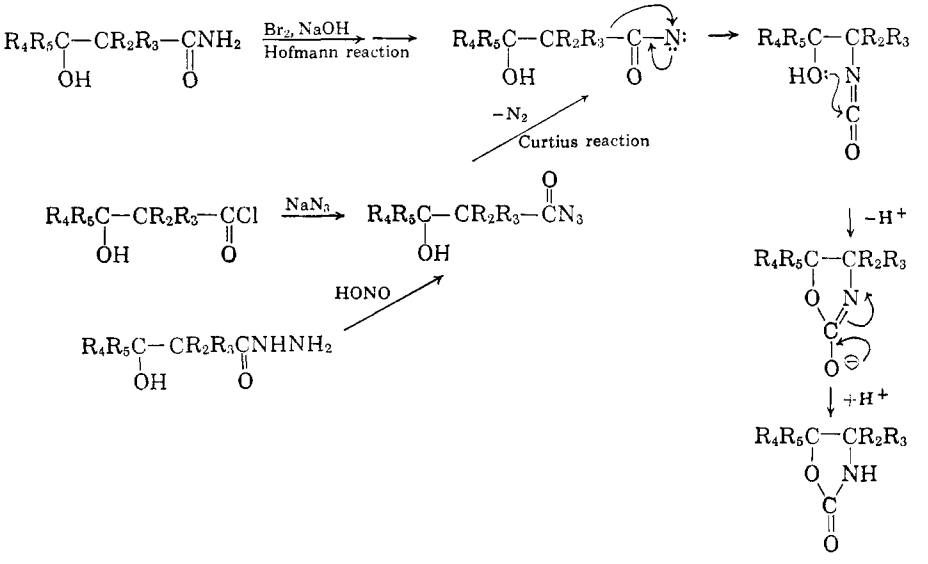
R = Me, mp 281–283°, 84% yield
R = H, mp 269–272°, 74% yield

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).

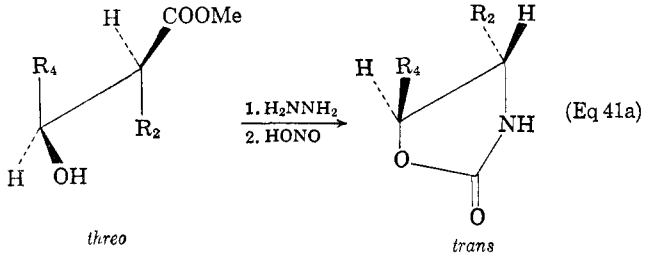
L. FROM β-HYDROXY ISOCYANATES (TABLE XXXIII)

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.

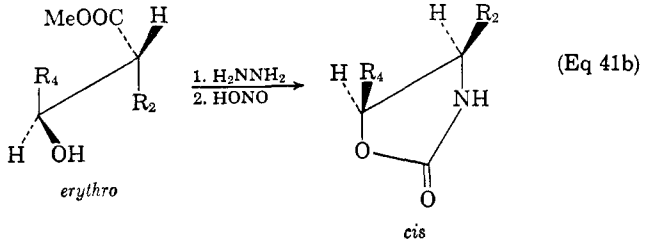


(Eq 40)

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



(Eq 41a)

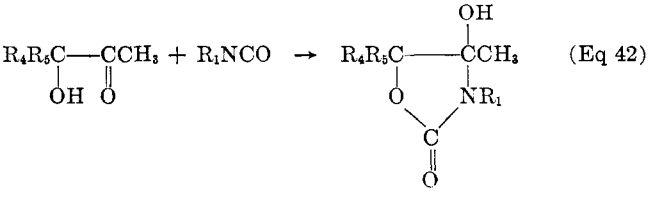


(Eq 41b)

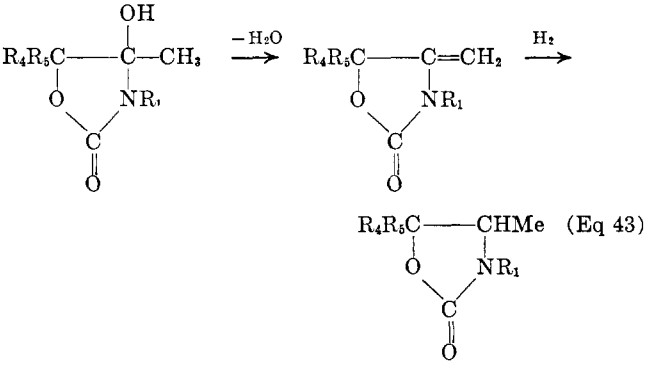
M. FROM ACYLOINS (α-KETOLS)

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).



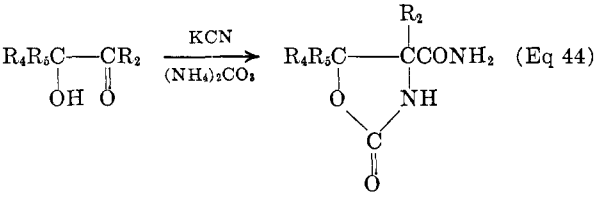
(Eq 42)



(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



(Eq 44)

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

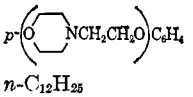
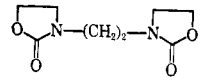
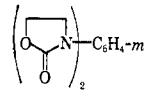
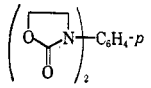
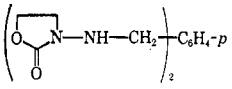
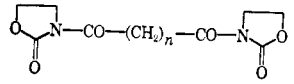
Empirical formula[a]	R_1	R_2	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_3H_5NO_2$	H	H	H	90	...	459
$C_3H_6N_2O_2$	H_2N	H	H	70 (EtOH), 34	...	119, 170
$C_4H_5NO_4$	H	HOOC	H	118	...	448
$C_4H_7NO_2$	Me	H	H	71 (HCl salt)	...	123
	Me	H	H	208 dec (MeCl salt)	...	123
	H	H	Me	89–90 (0.04)	...	367
$C_5H_7NO_2$	CH_2=CH	H	H	100–105 (1.3)	...	23
$C_5H_8NO_2Cl$	$ClCH_2CH_2$	H	H	122–124 (1)	72	23
$C_5H_{10}N_2O_2$	Me_2N	H	H	72 (Et_2O)	87	116
$C_6H_9NO_2$	CH_2=$CHCH_2$	H	H	...	Poor	420
$C_6H_{11}NO_2$	H	H	*i*-Pr	113–114 (*d* form)	...	375
$C_7H_{13}NO_2$	*n*-Bu	H	H	122 (4)	80	395
	t-Bu	H	H	94 (2)	62	395
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	246–247, 255–256	83	170, 403, 566
$C_8H_{16}N_2O_2$	$Me_2N(CH_2)_3$	H	H	117, 177 (hygroscopic)	...	120, 122
$C_9H_7NO_2Cl$	3,4-$Cl_2C_6H_3$	H	H	79	...	380
$C_9H_7N_2O_5Cl$	2-HO-3-NO_2-5-ClC_6H_2	H	H	...	...	497
$C_9H_8NO_2Cl$	*m*-ClC_6H_4	H	H	53.0–53.5	95	279, 341
	p-ClC_6H_4	H	H	120.9–121.5, 122.5	92	279, 341, 395
$C_9H_8NO_2Br$	*o*-BrC_6H_4	H	H	142–147 (0.01)	76	341
	p-BrC_6H_4	H	H	139.8–140.6	96	341
$C_9H_8NO_3Cl$	2-HO,5-ClC_6H_3	H	H	186	...	497
$C_9H_8N_2O_4$	*p*-$O_2NC_6H_4$	H	H	154.5	95	395
	o-$O_2NC_6H_4$	H	H	110	97	395
$C_9H_9NO_2$	Ph	H	H	118 (C_6H_6), 121–122	95	395, 492
$C_9H_9N_2O_3Cl$	2-HO-3-H_2N-5-ClC_6H_2	H	H	...	...	497
$C_{10}H_9NO_2Cl_2$	*p*-ClC_6H_4	H	$ClCH_2$	126.5	93	279
$C_{10}H_{10}NO_2Cl$	*p*-ClC_6H_4	H	Me	114	94	279
	Ph	$ClCH_2$	H	73–78 (ligroin)	...	277
	Ph	H	$ClCH_2$	108	95	277, 279
$C_{10}H_{10}NO_3Cl$	H	H	*o*-$ClC_6H_4OCH_2$	151	...	36
$C_{10}H_{10}N_2O_2$	PhCH=N	H	H	141–143	...	566
$C_{10}H_{11}NO_2$	$PhCH_2$	H	H	79.5–80.0	96	123, 341
	o-MeC_6H_4	H	H	125–130 (0.001), 170 (4)	80	341, 395
	m-MeC_6H_4	H	H	94.3–95.0	78	341
	p-MeC_6H_4	H	H	90.5–91.0	70	341, 395
$C_{10}H_{11}NO_3$	*m*-$MeOC_6H_4$	H	H	77–77.6	72	341
	p-$MeOC_6H_4$	H	H	109–110	93	341
$C_{10}H_{18}N_2O_3$	N-Morpholinopropyl	H	H	171 (*n*-BuOH) (hygroscopic) (HCl salt)	...	122
$C_{10}H_{20}N_2O_2$	$Et_2N(CH_2)_3$	H	H	...	...	122
$C_{11}H_{11}N_2O_3Cl$	PhNHCO	H	$ClCH_2$	154–155 (alc)	...	276
$C_{11}H_{12}NO_3Cl$	H	H	3-Cl-6-$MeC_6H_3OCH_2$	104–104.5, 200 (0.1)	...	318
$C_{11}H_{13}NO_2$	*p*-MeC_6H_4	H	Me	67.5	93	279
$C_{11}H_{13}NO_3$	H	H	*o*-$MeC_6H_4OCH_2$	125.6–126.5	...	36
	p-$EtOC_6H_4$	H	H	94–95	92	341
$C_{11}H_{13}NO_4$	H	H	*o*-$MeOC_6H_4OCH_2$	140–144, 220–225 (0.1)	...	36, 318
$C_{12}H_{13}NO_4$	*p*-$EtOCOC_6H_4$	H	H	110	97	395
$C_{12}H_{13}N_2O_3Cl$	$PhCH_2NHCO$	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-Naphthyloxymethyl	193.0–193.6	...	36
$C_{15}H_{12}NO_2Cl$	*p*-ClC_6H_4	H	Ph	131	96	279
$C_{15}H_{13}NO_2$	Ph	H	Ph	129	97	279
$C_{15}H_{20}N_2O_4$		H	H	...	...	369
$C_{15}H_{29}NO_2$	*n*-$C_{12}H_{25}$	H	H	62 (EtOH)	52	531
$C_{17}H_{16}N_2O_4$	1-Anthraquinonyl	H	H	226.5	85	395

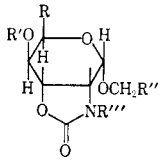
TABLE XXXI (*Continued*)

Empirical formula[a]	Structure	R_1	R_2	R_4	Bp (mm) or mp, °C	% yield	Ref
$C_{17}H_{16}N_2O_4$		Ph	H	$PhNHCOOCH_2$	...	...	265
					107	80	395
					175	62	395
					253	68	395
					96 (MeOH)	...	163
				$n = 0$	238 (HOAc)	47	117, 366
				$n = 1$	169 (HOAc)	78	117, 366
				$n = 2$	193.5 (HOAc)	72	366
				$n = 4$	138 (HOAc)	26	117, 366
				$n = 8$	130–131 (HOAc)	82	366

[a] $R_3 = R_5 = H$.

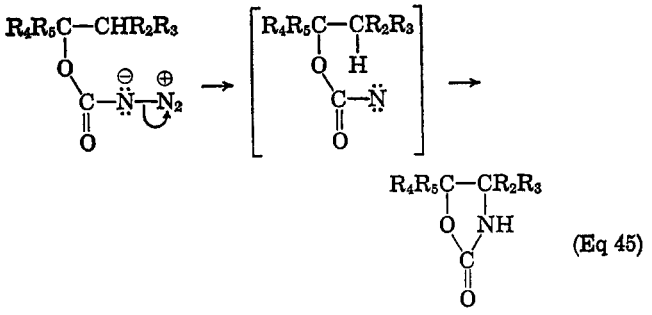
TABLE XXXII

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
$C_{15}H_{19}NO_6$	$PhCH_2OCH_2$	H	H	H	114 (MeOH–*i*-PrOH)	90	211
$C_{16}H_{18}N_4O_6$	N_3CH_2	CH_3CO	Ph	H	...	..	210
$C_{17}H_{21}NO_9S$	$MeSO_3CH_2$	CH_3CO	Ph	H	177	..	210
$C_{19}H_{23}NO_8$	$PhCH_2OCH_2$	CH_3CO	CH_3CO	H	147 (MeOH–*i*-PrOH)	80	211
$C_{20}H_{25}NO_9$	$PhCH_2OCH_2$	CH_3CO	CH_3CO	CH_3CO	99–100 (THF–*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.

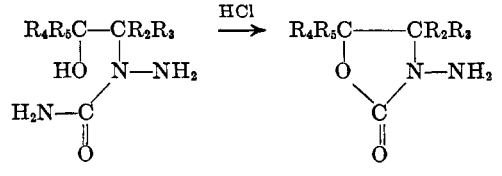


(Eq 45)

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)



(Eq 46)

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
$C_4H_7NO_3$	H	MeO	H	H	H	...	..	462
$C_5H_9NO_2$	H	H	H	Me	Me	56.8–58 (alc–Et_2O)	13	97
$C_6H_{11}NO_2$	H	H	H	*i*-Pr	H	(*l*) 113–114 (C_6H_6)	...	375, 376
$C_7H_{13}NO_2$	H	*i*-Bu	H	H	H	130–140 (0.2)	28	386
	H	Et	Et	H	H	160–170 (0.6)	30	386
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	H	H	256–257 (DMF)	93	1, 219
$C_8H_{13}NO_2$	H	H	H	—$(CH_2)_5$—		101.0–102.4	82	381
$C_9H_9NO_2$	H	Ph	H	H	H	137–139	40	386
	H	H	H	Ph	H	89–90 (H_2O), 88–90 (alc–Skellysolve B)	50	21, 97
$C_9H_{13}NO_2$	H	H	H		H	103–104	72	209
$C_9H_{15}NO_2$	H	H	H	—$(CH_2)_4$CHMe—		110	...	434
	H	H	H	—$(CH_2)_2$CHMe$(CH_2)_2$—		131	...	434
	H	H	H	—$(CH_2)_3$CHMeCH_2—		118–120	...	434
$C_9H_{15}NO_3$	H	H	H	—$(CH_2)_2$CH(OMe)$(CH_2)_2$—		135	...	434
$C_9H_{15}NO_4$	H	H	H	 OH (*trans*)	H	...	...	209
$C_{13}H_{10}N_2O_4$	H	PhOCONH	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	*p*-$MeOC_6H_4$	H	108–109 (EtOH)	93	55
	H	H	H	*m*-$MeOC_6H_4$	H	202–203 (BuOH)	25	55
$C_{10}H_{17}NO_2$	H	H	H	—CH_2CHMeCH_2CHMeCH_2—		120	...	434
	H	H	H	—CH_2CHMeCHMe$(CH_2)_2$—		103	...	434
	H	H	H	—$(CH_2)_3$CHEtCH_2—		109	...	434
	H	H	H	—$(CH_2)_3$CMe_2CH_2—		148	...	434
	H	H	H	—$(CH_2)_7$—		127	...	434
$C_{11}H_{12}N_2O_2$	$PhCH_2CH$=N	H	H	H	H	251–256	...	219
$C_{11}H_{12}N_2O_3$	H	$PhCH_2CONH$	H	H	H	(*dl*) 184 (H_2O)	78	37
						(*d*) 157 (H_2O)	77	37
						(*l*) 157 (H_2O)	73	37
$C_{11}H_{12}N_2O_4$	H	$PhCH_2OCONH$	H	H	H	(*dl*) 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	(*dl*) *cis*, 134–135 (C_6H_6–Et_2O)	60	7
$C_{11}H_{13}NO_4$	H	H	H	2,5-$(MeO)_2C_6H_3$	H	107 (C_6H_6)	...	41
$C_{12}H_{15}NO_2$	H	Ph	*i*-Pr	H	H	139–140	74	386
$C_{12}H_{15}NO_4$	H	H	H	2,5-$(MeO)_2C_6H_3$	Me	159 (C_6H_6)	...	41
$C_{13}H_{17}NO_4$	H	H	H	2,5-$(EtO)_2C_6H_3$	H	86.5 (C_6H_6–hexane)	...	257
$C_{13}H_{21}NO_2$	H	H	H	*trans*-2-Decahydronaphthyl	H	165 and 200	...	434
	H	H	H	*cis*-2-Decahydronaphthyl	H	140 and 207	...	434
$C_{15}H_{13}NO_2$	H	H	H	Ph	Ph	200 (EtOH)	...	75
	H	Ph	H	Ph	H	*cis*, 193.5–194.5; *trans*, 161–162	...	611
	H	Ph	Ph	H	H	178–179	63	386
$C_{16}H_{15}NO_2$	H	Ph	$PhCH_2$	H	H	106–107	62	386
$C_{16}H_{15}NO_3$	H	H	H	*p*-$PhCH_2OC_6H_4$	H	145–146 (EtOH)	76	55
	H	H	H	*m*-$PhCH_2OC_6H_4$	H	106–107 (EtOH)	76	55
$C_{17}H_{17}NO_3$	H	H	H	2-$PhCH_2O$-5-MeC_6H_3	H	150–150.5 (C_6H_6–hexane)	...	22
$C_{21}H_{25}NO_6$	H	H	H	3,4-$(MeO)_2C_6H_3CH_2$	3,4-$(MeO)_2$-$C_6H_3CH_2$	161 (MeOH)	86	472
Name								
4-Dihydrolysergylamido-2-oxazolidone						(*d*) 233–235 (MeOH), (*l*) 244–246 (MeOH)	...	505

Table XXXIII (*Continued*)

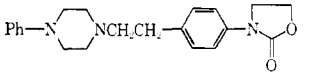
Name or structure	Bp (mm) or mp, °C	% yield	Ref
4-Dihydrolysergylamido-5,5-dimethyl-2-oxazolidone	(*d*) 268–270 (Me_2CO), (*l*) 280 (MeOH)	...	505
	194–196	14	333
 R = 8-Hydroxy-6-sulfonaphth-2-yl	...	...	498
7-Hydroxynaphth-1-yl	218–219 (H_2O)	...	498
5-Hydroxy-7-sulfonaphth-2-yl	...	...	498
6-Hydroxy-8-sulfonaphth-2-yl	...	...	498
5-Hydroxy-1,7-disulfonaphth-2-yl	...	...	498
8-Hydroxy-3,6-disulfonaphth-2-yl	...	...	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
$C_{12}H_{12}NO_2Cl$	*p*-ClC_6H_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
$C_{12}H_{14}NO_2Cl$	*p*-ClC_6H_4	Me	H	Me	Me	...	..
$C_{12}H_{14}NO_3Cl$	*p*-ClC_6H_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	...	..
$C_{13}H_{14}NO_2Cl$	*p*-ClC_6H_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
$C_7H_{11}NO_4$	HOCO	Me		Me	206–207	74
$C_7H_{12}N_2O_3$	H_2NCO	Me		Me	208–209	34
$C_8H_{13}NO_4$	HOCO	Me		Et	206–207	80
	MeOCO	Me		Me	99–100	58
$C_8H_{14}N_2O_3$	H_2NCO	Me		Et	224–226	31
$C_9H_{15}NO_4$	HOCO	Et		Et	177–179	66
$C_9H_{16}N_2O_3$	H_2NCO	Et		Et	175–177	72
$C_{10}H_{15}NO_4$	HOCO		—$(CH_2)_5$—		205–206	73
$C_{10}H_{16}N_2O_3$	H_2NCO		—$(CH_2)_5$—		253–254	79
$C_{10}H_{17}NO_4$	HOCO	Me		*i*-Bu	186–187[b]	74
	HOCO	Me		*i*-Bu	195–196[b]	69
$C_{10}H_{18}N_2O_3$	H_2NCO	Me		*i*-Bu	192–194[b]	39
	H_2NCO	Me		*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*-Bu	89–90	69
$C_{12}H_{13}NO_4$	HOCO	Me		Ph	198–199	72
$C_{12}H_{14}N_2O_3$	H_2NCO	Me		Ph	222–224	24

[a] R_1 = H; R_2 = 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
$C_3H_5NO_2$	H	H	H	H	...	..	296
$C_4H_7NO_2$	H	H	Me	H	...	..	296
$C_5H_9NO_2$	H	H	Me	Me	80–81	75	295, 296, 431
$C_6H_{11}NO_2$	Et	Me	H	H	...	68	482, 600

[a] R_1 = H.

TABLE XXXVII

2-OXAZOLIDONES FROM 2-OXAZOLINES AND WATER

Empirical formula[a]	R_2	R_3	R_4	Mp, °C	% yield	Ref
$C_{12}H_{12}NO_4Cl$	p-$ClC_6H_4COOCH_2$	Me	H	117	..	441, 442
$C_{13}H_{15}NO_4$	p-$MeC_6H_4COOCH_2$	Me	H	169 (H_2O)	..	441, 442
$C_{13}H_{15}NO_5$	p-$MeOC_6H_4COOCH_2$	Me	H	86 (H_2O)	..	441
$C_{15}H_{19}NO_6$	$3,4,5$-$(MeO)_3C_6H_2COOCH_2$	Me	H	144–145 (H_2O)	..	441, 442
$C_{17}H_{15}NO_4$	$PhCOOCH_2$	H	Ph	87–87.5 (EtOH–hexane)	4	426

[a] $R_1 = R_5 = H$.

TABLE XXXVIII

2-OXAZOLIDONES FROM 2-IMINOOXAZOLIDINES

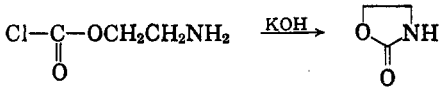
Empirical formula[a]	R_1	R_2	R_4	Mp, °C	Ref
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	253–256	154
$C_9H_9N_3O_5$	5-Nitro-2-furfurylideneamino	H	Me	245–248	154
	5-Nitro-2-furfurylideneamino	Me	H	199–200	154
$C_{10}H_9N_3O_5$	3-(5-Nitro-2-furyl)acrylideneamino	H	H	270	154
$C_{11}H_{12}N_2O_2S$	PhNHCS	H	Me	114 (EtOH)	183
$C_{11}H_{12}N_2O_5S$	p-$MeCONHC_6H_4SO_2$	H	H	175	272
$C_{11}H_{13}NO_2$	Me	Me	Ph	...	176
$C_{12}H_{15}N_3O_5$	5-Nitro-2-furfurylideneamino	H	Bu	194	154
$C_{15}H_{18}N_2O_2S_2$	CH_2=$CHCH_2NHCS$	H	$PhCH_2SCH_2$	59 (EtOH)	183
$C_{19}H_{20}N_2O_2S_2$	PhNHCS	H	$PhCH_2SCH_2$	107 (EtOH)	183

[a] $R_3 = R_5 = H$.

(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.

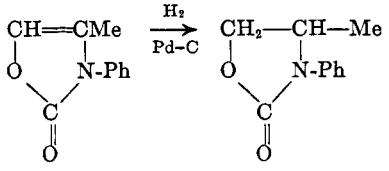


(Eq 47)

mp 90°
bp 152°(0.4 mm)

Q. FROM OXAZOLINES AND OXAZOLINONES (TABLE XXXVII)

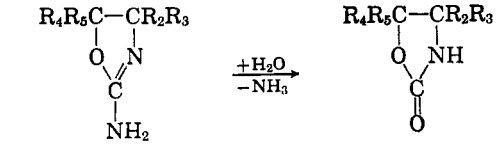
In one case (477), an oxazolinone was reduced to an oxazolidone with hydrogen at atmospheric pressure and room temperature employing a palladium-on-carbon catalyst (Eq 48).



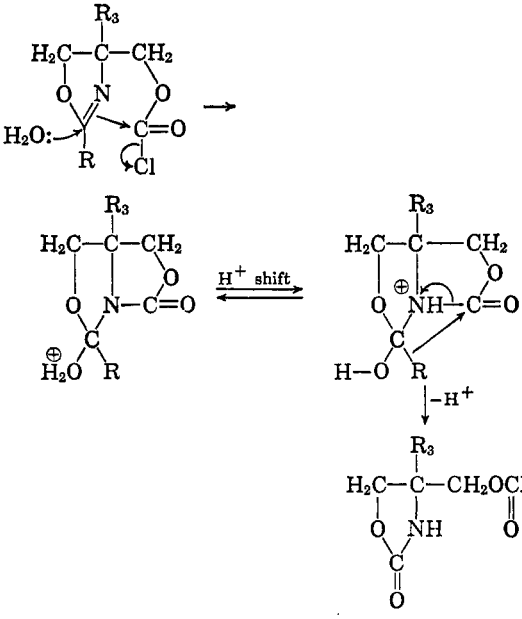
(Eq 48)

mp 52–52.5° (Et_2O)

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).



(Eq 49)



(Eq 50)

R. FROM 2-IMINOOXAZOLIDINES (TABLE XXXVIII)

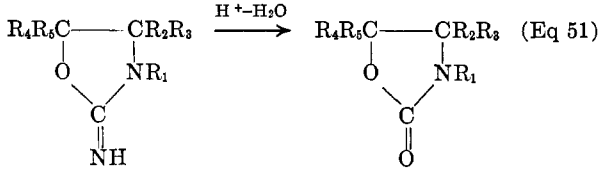
2-Iminooxazolidines are converted to 2-oxazolidones by hydrolysis with sulfuric or nitrous acid (154, 176) (Eq 51)

TABLE XXXIX

2-OXAZOLIDONES (MISCELLANEOUS)

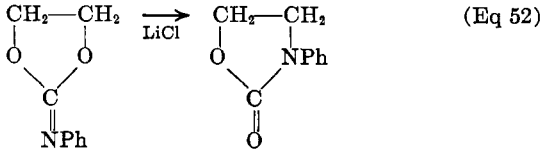
Empirical formula	R_1	R_2	R_3	R_4	R_5	Mp, °C	% yield	Ref
$C_4H_7NO_2$	H	H	H	Me	H	...	90	280
$C_9H_9N_2O_2SCl$	4-Cl-3-$(H_2NSO_2)C_6H_2$	H	H	H	H	182–183	..	280
$C_{11}H_{14}NO_3$	Me	H	H	*m*-$MeOC_6H_4$	H	Oily	..	527
	Me	H	H	*p*-$MeOC_6H_4$	H	72–75	..	527
$C_{13}H_{16}N_4O_3$	5-Nitro-2-furfurylidene-amino	H	H	N-Morpholino-methyl	H	205–206 (Me_2CO)	..	374
$C_{13}H_{22}N_2O_4Cl$	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_4CHCl$—		...	55	434
$C_{13}H_{22}N_2O_4$	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_5$—		HCl salt, 205 (EtOH)	72	434
$C_{14}H_{20}N_2O_2$	$Me_2NCH_2CH_2$	Me	H	Ph	H	(*cis*)	57	609
						(*trans*)	50	609
$C_{14}H_{25}N_2O_4$	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_4CHMe$—		...	67	434
	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_2CHMe(CH_2)_2$—		...	89	434
	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_3CHMeCH_2$—		...	61	434
$C_{14}H_{25}N_2O_5$	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_2CH(OMe)(CH_2)_2$—		...	42	434
	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_4CH(OMe)$—		...	40	434
$C_{14}H_{26}N_2O_3$	$Me_2N(CH_2)_2NHCO$	H	H	—$(CH_2)_3CHMeCH_2$—		...	34	434
$C_{15}H_{27}N_2O_4$	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_7$—		...	70	434
	$Me_2N(CH_2)_2OCO$	H	H	—$CH_2CHMeCH_2CHMeCH_2$—		...	82	434
	$Me_2N(CH_2)_2OCO$	H	H	—$CH_2CHMeCHMe(CH_2)_2$—		...	75	434
	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_2CHEt(CH_2)_2$—		...	75	434
	$Me_2N(CH_2)_2OCO$	H	H	—$(CH_2)_2CMe_2(CH_2)_2$—		...	73	434
$C_{16}H_{29}N_2O_4$	$Et_2N(CH_2)_2OCO$	H	H	—$(CH_2)_3CHMeCH_2$—		...	56	434
$C_{17}H_{17}NO_3$	Me	H	H	*m*-$PhCH_2OC_6H_4$	H	65–66 (EtOH)	50	527
	Me	H	H	*p*-$PhCH_2OC_6H_4$	H	101–102	..	527
$C_{17}H_{17}NO_4$	*p*-$MeOC_6H_4CH_2$	Me	H	Ph	H	*cis*	70	609
						trans	75	609
	$PhOCH_2CH_2$	Me	H	Ph	H	*cis*, 55–57	51	609
						trans, 113–115	54	609
$C_{18}H_{30}N_2O_4$	$Me_2N(CH_2)_2OCO$	H	H	*trans*-2-Decahydronaphthyl	H	...	60	434
	$Me_2N(CH_2)_2OCO$	H	H	*cis*-2-Decahydronaphthyl	H	...	77	434
$C_{21}H_{19}NO_2$	α-Naphthylmethylene	Me	H	Ph	H	*cis*, 117–118	55	609
						trans, 120–125	57	609

Structure	R			
	*m*-$CF_3C_6H_4$—N⟨⟩N—$(CH_2)_2C_6H_4$-*p*	125–126	..	334
	m-$MeSO_2C_6H_4$—N⟨⟩N—$(CH_2)_2C_6H_4$-*p*	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.

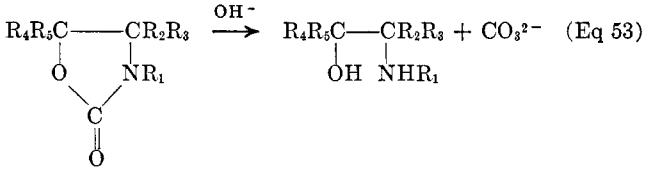
III. REACTIONS OF 2-OXAZOLIDONES

A. DECOMPOSITION AND RING-OPENING REACTIONS

1. Reactions with Bases

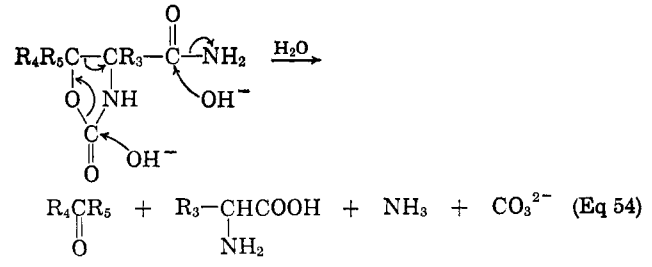
a. With Hydroxylic Bases

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


(Eq 53)

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).

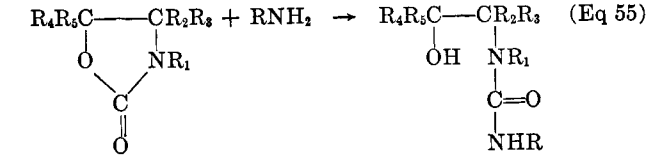

(Eq 54)

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).

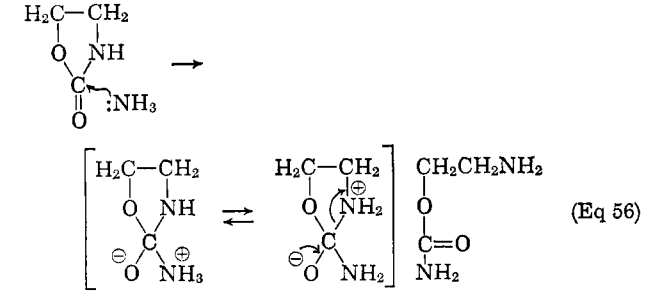
c. With Nitrogenous Bases and Ammonia

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)


(Eq 55)

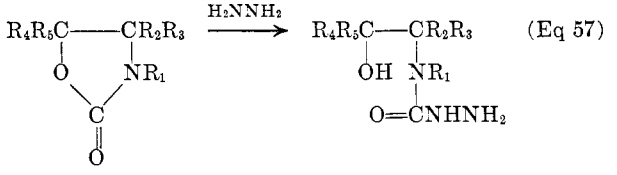
When aromatic primary amines or araliphatic amines are used, such as benzylamine, the products of ring opening are an N,N′-disubstituted urea and a 2-imidazolidone.

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


(Eq 56)

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).


(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-) aninoethyl 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)

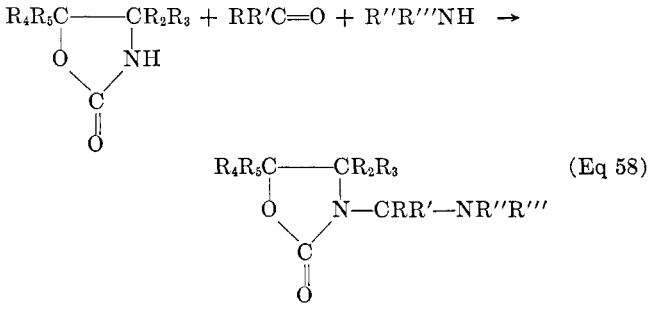
The endocyclic nitrogen has been acylated in both acidic (309) and basic (250) media. Carbamylation has been effected by reaction with phosgene in basic medium, followed by reaction with ammonia (97).

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)

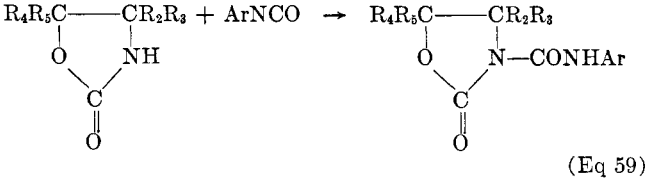
2-Oxazolidones react with carbonyl compounds in the presence of added amine in a manner analogous to the Mannich reaction (34) (Eq 58). In the absence of added amine, a second molecule of oxazolidone serves as the amine (Eq 58, R″R‴NH = $\overline{\text{OCOCH}_2\text{CH}_2\text{N}}$–). In one recorded instance a hydroxy compound is produced (57).



(Eq 58)

5. Reaction with Aryl Isocyanates (Table XLIV)

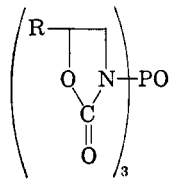
Reaction of substituted 2-oxazolidones with aryl isocyanates in the presence of pyridine or triethylamine yields 2-oxazolidone-3-carbanilides (Eq 59) (487).



(Eq 59)

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)



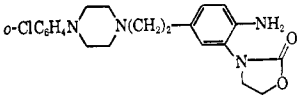
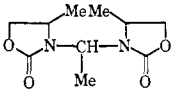
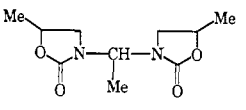
R = H, Me or Et

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
$C_5H_7NO_2$	CH_2=CH	H	H	H	76.5–78.0 (0.5), 90–96 (1-2)	28	586, 586a
$C_5H_9NO_3$	$HOCH_2CH_2$	H	H	H	...	..	332
$C_6H_6N_2O_2$	NCCH=CH	H	H	H	...	..	468
$C_6H_7NO_2$	HC≡CCH_2	H	H	H	68–69 (0.39–0.40)	..	535
$C_6H_8N_2O_2$	$NCCH_2CH_2$	H	H	H	Oil	93	326
$C_6H_9NO_2$	CH_2=CH	H	Me	H	78–81 (1.3) 105–108 (2.5)	86	38, 413, 586, 586a
$C_6H_{11}NO_2$	Me	H	Me	Me	128–132 (24)	51	97
$C_7H_9NO_2$	HC≡CCH_2	H	Me	H	35–36 (EtOH–H_2O)	..	535
$C_7H_{11}NO_2$	CH_2=$CHCH_2$	H	Me	H	80 (0.4)	..	539
	CH_2=CH	H	Et	H	82–90 (0.7)	45	586
$C_8H_{13}NO_2$	CH_2=$CHCH_2$	H	Et	H	...	..	539
	CH_2=$CHCH_2$	H	Me	Me	...	..	539
$C_8H_{15}NO_2$	Me	H	Et	Et	92–94 (0.3)	68	97
$C_9H_{18}N_2O_2$	Me	H	Et_2NCH_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
$C_{11}H_{12}NO_3Cl$	Me	H	*o*-$ClC_6H_4OCH_2$	H	79–81	..	12
	Me	H	*m*-$ClC_6H_4OCH_2$	H	...	..	12
$C_{11}H_{13}NO_3$	Me	H	*p*-$MeOC_6H_4OCH_2$	H	75 (Et_2O)	78	55
	Me	H	*m*-$MeOC_6H_4OCH_2$	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	*m*-$MeC_6H_4OCH_2$	H	73.5	..	12
$C_{12}H_{16}NO_4$	Me	H	*o*-$MeOC_6H_4OCH_2$	H	72.5–75 (C_6H_6–Et_2O)	..	12
	Me	H	*p*-$MeOC_6H_4OCH_2$	H	...	..	12
$C_{12}H_{15}NO_5$	Me	H	3,4-$(MeO)_2C_6H_3$	H	...	..	419
$C_{13}H_{17}NO_4$	Et	H	*o*-$MeOC_6H_4OCH_2$	H	175–178 (0.1)	..	12
$C_{16}H_{21}N_2O_2$	β-N-Pyrrolidinoethyl	Me	Ph	H	*trans*, 126–128	..	610
$C_{16}H_{22}N_2O_3$	β-N-Morpholinoethyl	Me	Ph	H	*cis*, 86–89; *trans*, 60–62	..	610
$C_{17}H_{17}NO_3$	Me	H	*p*-$PhCH_2OC_6H_4$	H	101–102 (EtOH)	76	55
	Me	H	*m*-$PhCH_2OC_6H_4$	H	65–66 (dil EtOH)	80	55
$C_{17}H_{23}N_2O_2$	β-N-Piperidinoethyl	Me	Ph	H	*cis*, 95–96; *trans*, 49–52	..	610
$C_{20}H_{28}NO_6$	Me	H	3,4-$(MeO)_2C_6H_3$	3,4-$(MeO)_2C_6H_3$	118–120 (Et_2O–MeOH)	96	472
Structure							
					168–169 (*i*-PrOH)	..	30
					223.5	74	241
					198–199 (Me_2CO)	7	576

[a] R_3 = 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
$C_5H_7NO_3$	MeCO	H	H	H	H	69–70 (Skellysolve B–Et_2O)	..	250
$C_6H_9NO_2$	CH_2=CH	H	H	Me	H	...	14	309
$C_6H_{10}N_2O_3$	H_2NCO	H	H	Me	Me	118–120 (EtOH)	48	97
$C_7H_{11}NO_3$	MeCO	H	H	Me	Me	42.5–44 (EtOH–Skellysolve B)	75	97
$C_8H_{13}NO_4$	EtOCO	H	H	Me	Me	54–55.5 (Et_2O–Skellysolve B)	79	97
$C_8H_{14}N_2O_3$	H_2NCO	H	H	Et	Et	82–84 (C_6H_6–Skellysolve B)	78	97
$C_9H_{14}NO_3$	Me_3CCO	H	H	Me	Me	80–81 (Skellysolve B)	48	97
$C_9H_{16}N_2O_3$	H_2NCO	Me	Me	Pr	H	102–105 (EtOH)	55	97
$C_{10}H_{10}N_2O_3$	H_2NCO	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_2CHCH_2CO	H	H	Me	Me	49.5–51 (Skellysolve B)	70	97
$C_{11}H_{12}N_2O_3$	H_2NCO	H	H	Ph	Me	113–114 (EtOH)	54	97
$C_{12}H_{14}N_2O_3$	H_2NCO	H	H	Ph	Et	112–113 (C_6H_6–Skellysolve B)	63	97
$C_{16}H_{14}N_2O_3$	H_2NCO	H	H	Ph	Ph	181–185 (EtOH)	68	97
$C_{17}H_{15}NO_3$	MeCO	H	H	Ph	Ph	142–143 (EtOH)	76	97
	Structure					99–100 (THF–*i*-Pr_2O)	88	211

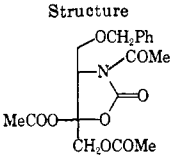


TABLE XLII

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

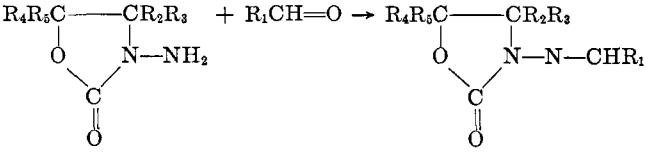
Empirical formula	R_1	R_2	R_3	R_4	R_5	Bp (mm) or mp, °C	% yield	Ref
$C_3H_4N_2O_3$	ON	H	H	H	H	100	..	383, 425
$C_3H_4N_2O_4$	O_2N	H	H	H	H	...	..	195
$C_3H_6N_2O_2$	H_2N	H	H	H	H	69–71 (EtOH)	55	195, 425
$C_5H_6N_4O_{10}$	O_2N	O_2NOCH_2	O_2NOCH_2	H	H	122–123	30	60
$C_6H_8N_2O_3$	ON	H	H	Me	Me	87.9–89.8	71	383
	ON	Me	Me	H	H	95.8–96.4	70	156, 382
	ON	Et	H	H	H	110 (1)	84	156, 382
$C_6H_8N_2O_4$	O_2N	Me	Me	H	H	...	..	201
$C_5H_{10}N_2O_2$	H_2N	Me	Me	H	H	130–135 (10)	..	201
$C_7H_{12}N_2O_3$	ON	H	H	Et	Et	...	..	383
$C_8H_{12}N_2O_3$	ON	H	H	$-(CH_2)_5-$		82.5–83.2	94	381, 383
	ON	$-(CH_2)_5-$		H	H	107.5–108.5	99	156, 382
$C_9H_8N_2O_3$	ON	Ph	H	H	H	83.8–84.6	80	156, 382
	ON	H	H	Ph	H	76.5–77.5	77	383
$C_9H_{12}N_2O_8$	O_2N	$MeCOOCH_2$	$MeCOOCH_2$	H	H	97.1–97.8	..	90
$C_9H_{14}N_2O_3$	ON	H	H	$-(CH_2)_6-$		82.6–83.5	93	383
$C_{10}H_{10}N_2O_3$	ON	H	H	Ph	Me	116.5–117.4	97	383
	ON	Ph	Me	H	H	84.6–86.0	98	156, 382
$C_{11}H_{12}N_2O_3$	ON	H	H	Ph	Et	...	..	383
$C_{15}H_{13}N_2O_3$	ON	H	H	Ph	Ph	107.5–108.5	92	383
	ON	Ph	H	Ph	H	*erythro*, 115.2–117.5	89	383
						threo, 106.5–108.0	91	383
	ON	Ph	Ph	H	H	100.2–101.0	91	156, 382
$C_{23}H_{17}N_2O_2$	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 ($ZnCl_2$) (418).

Besides the free carbonyl compounds, the diacetate (234, 307, 402) and the oxime (204) have been used. Reactions have also been conduced on benzylideneamino (142), methyleneamino (234, 402), and acetylamino derivatives (234) of the oxazolidone.

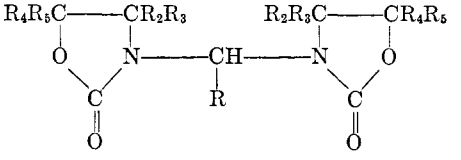


(Eq 60)

TABLE XLIII

REACTION PRODUCTS OF 2-OXAZOLIDONES WITH CARBONYL COMPOUNDS

Empirical formula[a]	Substitution at 3-position	Bp (mm) or mp, °C	% yield	Ref
$C_5H_6NO_3Cl_3$[b]	$Cl_3CCH(OH)$	134–136 (CCl_4)	..	57
$C_6H_{12}N_2O_2$	Me_2NCH_2	90 (0.2)	84	34
$C_8H_{14}N_2O_2$	N-Pyrrolidinomethyl	123 (0.2)	..	34
$C_8H_{16}N_2O_2$	Et_2NCH_2	107 (0.2)	80	34
$C_{12}H_{24}N_2O_2$	Bu_2NCH_2	130–132 (0.4)	80	34
$C_{13}H_{19}N_2O_2$	$PhCH_2N(Me_2)CH_2$	152	..	34



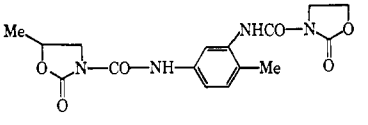
Empirical formula[c]	R	R_4	Mp, °C	% yield	Ref
$C_7H_{10}N_2O_4$	H	H	99–100 (EtOAc)	91	258
$C_8H_{12}N_2O_4$	Me	H	...	..	258
$C_9H_8N_2O_4Cl_6$	H	Cl_3C	129–134 (H_2O)	55	258
$C_9H_{10}N_2O_6$	H	OCH	197 dec	..	258
$C_9H_{14}N_2O_4$	H	Me	152–155	93	258
$C_{10}H_{16}N_2O_4$	Me	Me	195.5–198.5 (MeOH)	..	258
$C_{11}H_{16}N_2O_4$	H	CH_2=CH	Oil	..	258
$C_{11}H_{18}N_2O_4$	H	Et	123–126	..	258
$C_{13}H_{18}N_2O_4$	H	MeCH=CH	Oil	..	258
$C_{15}H_{16}N_2O_6$	H	2-furyl	138–141	..	258
$C_{15}H_{26}N_2O_4$	H	*n*-Bu	96–98	..	258
$C_{19}H_{18}N_2O_4$	H	Ph	125–127 (MeOH)	..	258
$C_{23}H_{22}N_2O_4$	H	PhCH=CH	128	..	258

[a] $R_2 = R_3 = R_4 = R_5 = H$. [b] No added amine. [c] $R_2 = R_3 = R_5 = H$.

TABLE XLIV

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

Empirical formula[a]	R_4	R_5	Ar	Mp, °C	% yield
$C_{10}H_{10}N_2O_3$	H	H	Ph	114–115	82
$C_{11}H_{11}N_2O_3Cl$	H	Me	*p*-ClC_6H_4	130–132	40
$C_{11}H_{12}N_2O_3$	H	Me	Ph	139–140	76
$C_{11}H_{12}N_2O_4$	H	H	*p*-$MeOC_6H_4$	143–144	50
$C_{12}H_{14}N_2O_3$	Me	Me	Ph	152–153	69
	H	Et	Ph	113–114	57
$C_{12}H_{14}N_2O_4$	H	Me	*p*-$MeOC_6H_4$	138–139	37
	Structure			195–197	..



[a] $R_2 = R_3 = H$.

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

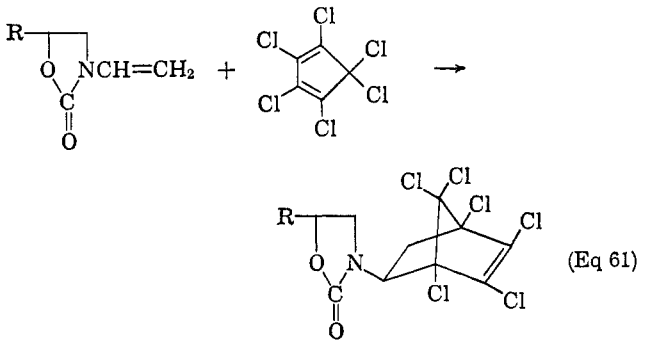
N-β-Chloroethyl-2-oxazolidone has been dehydrohalogenated with sodium oxide in benzene (23) or with potassium *t*-butoxide (218) to give N-vinyl-2-oxazolidone: mp 15°, bp 70° (0.1 mm), 100–105° (1.3 mm). Pyrolysis of N-(β-acetoxyethyl)-2-oxazolidone (299) eliminates acetic acid, also giving the N-vinyl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

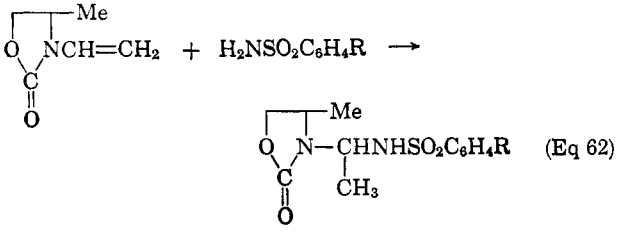
hexachlorocyclopentadiene yields the adducts shown in Eq 61 (438).



(Eq 61)

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).



(Eq 62)

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).

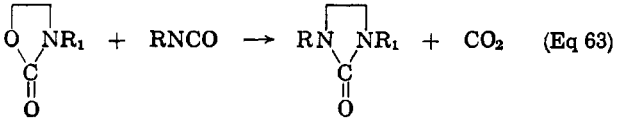
4. *Miscellaneous Reaction Products*

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.



(Eq 63)

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 mμ.

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 ephedrines (255).

TABLE XLV

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

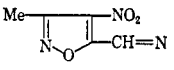
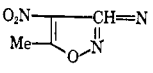
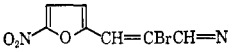
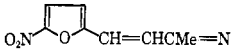
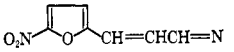
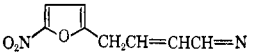
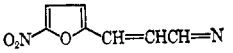
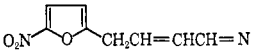
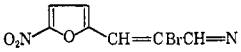
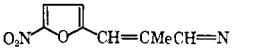
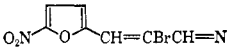
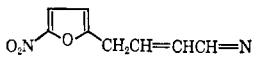
Empirical formula[a]	R_1	R_4	Mp °C	% yield	Ref
$C_4H_6N_2O_2$	CH_2=N	H	96 (MeOH)	..	233, 402
$C_5H_7N_2O_3Br$	5-Bromo-2-furfurylideneamino	H	179–182 (MeOH)	88	524
$C_5H_7N_2O_3I$	5-Iodo-2-furfurylideneamino	H	191–193 (MeOH)	90	524
$C_5H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	230, 246–248, 254–256 (*i*-PrOH)	96	71, 93, 142, 204, 234, 307, 402, 424, 425, 443, 558
$C_5H_6N_2O_5$		H	188–189 (aq EtOH)	..	85
		H	220–222 dec (EtOH)	..	85
$C_5H_5N_2O_3Cl$	5-Chloromethyl-2-furfurylidene-amino	H	159–162	90	275
$C_5H_{10}N_2O_3$	5-Methyl-2-furfurylideneamino	H	138–140 (50% MeOH)	71	524
$C_{10}H_9N_3O_5$	5(β-Nitrovinyl)-2-furfurylidene-amino	H	227–229 ($MeNO_2$)	58	275
$C_{10}H_9N_4O_5Br$		H	246–248 dec	..	301
$C_{10}H_{10}N_2O_4$	5-Aldehydo-2-furfurylideneamino	H	195–200 ($MeNO_2$)	61	275
$C_{11}H_{11}N_3O_5$		H	164–166.5 (EtOH)	96	418
	5(β-Nitro-β-methylvinyl)furfuryl-ideneamino	H	212–214 ($MeNO_2$)	20	275
$C_{11}H_{14}N_2O_4$	5-Ethoxymethyl-2-furfurylidene-amino	H	121 (EtOH)	..	275
$C_{13}H_{16}N_3O_4Br$	5-Bromo-2-furfurylideneamino	N-Morpholinomethyl	200–202 (MeOH)	84	522
$C_{13}H_{16}N_3O_4I$	5-Iodo-2-furfurylideneamino	N-Morpholinomethyl	209–210 (Me_2CO)	80	522
$C_{13}H_{16}N_4O_6$	5-Nitro-2-furfurylideneamino	N-Morpholinomethyl	204–206 (EtOH), 206–208	..	208, 522
$C_{13}H_{17}N_3O_4$	2-Furfurylideneamino	N-Morpholinomethyl	164–165 (MeOH)	84	522
$C_{13}H_{17}N_4O_5$		Me_2NCH_2	216–217	..	199
$C_{14}H_{13}N_4O_6$	As above	N-Morpholinomethyl	230–232	..	199
$C_{14}H_{19}N_3O_4$	5-Methyl-2-furfurylideneamino	N-Morpholinomethyl	182–183 (MeOH)	93	522
$C_{14}H_{19}N_4O_5$		Me_2NCH_2	120.5–121.5	..	199
$C_{15}H_{14}N_4O_5$		N-Pyrrolidinomethyl	211–212	..	199
$C_{15}H_{15}N_4O_6$		N-Morpholinomethyl	170–172	..	199
$C_{15}H_{18}N_3O_3Cl$	*o*-ClC_6H_4CH=N	N-Morpholinomethyl	122–123 (50% MeOH)	82	522
	p-ClC_6H_4CH=N	N-Morpholinomethyl	138–139 (50% MeOH)	53	522
$C_{15}H_{18}N_3O_3Br$	*o*-BrC_6H_4CH=N	N-Morpholinomethyl	129–130 (50% MeOH)	76	522
	p-BrC_6H_4CH=N	N-Morpholinomethyl	150–151 (50% MeOH)	84	522
$C_{15}H_{18}N_3O_3I$	*p*-IC_6H_4CH=N	N-Morpholinomethyl	195–198 (Me_2CO)	60	522
$C_{15}H_{18}N_4O_5$	*p*-$O_2NC_6H_4CH$=N	N-Morpholinomethyl	181–182 (MeOH)	95	522
	m-$O_2NC_6H_4CH$=N	N-Morpholinomethyl	174–175 (MeOH)	95	522
	5-Nitro-2-furfurylideneamino	N-Piperidinomethyl	197–198 (EtOH)	..	203
$C_{15}H_{18}N_5O_6Br$		N-Morpholinomethyl	202–205 dec 195–196 (dioxane)	..	225, 301
$C_{15}H_{19}N_3O_3$	PhCH=N	N-Morpholinomethyl	168–169 (MeOH)	68	522
$C_{15}H_{19}N_3O_4$	*o*-HOC_6H_4CH=N	N-Morpholinomethyl	191–192 (MeOH)	68	522
$C_{16}H_{20}N_3O_6Br$	3-Br-4-$MeOC_6H_4CH$=N	N-Morpholinomethyl	152–153 (50% Me_2CO)	87	522
$C_{16}H_{20}N_4O_6$		N-Morpholinomethyl	176–176.5 (C_6H_6–*i*-PrOH)	..	225
$C_{16}H_{21}N_3O_4$	*p*-$MeOC_6H_4CH$=N	N-Morpholinomethyl	149–150	70	522
$C_{17}H_{15}N_4O_6Br$		*o*-$MeOC_6H_4O$	182–184	..	301

TABLE XLV (*Continued*)

Empirical formula[a]	R_1	R_4	Mp °C	% yield	Ref
$C_{17}H_{22}N_4O_5$		N-Piperidinomethyl	151–152	..	199
	5-Nitro-2-furfurylideneamino	Bu_2NCH_2	152.5–153.5 (EtOH)	..	203

[a] $R_2 = R_3 = R_5 = H$.

TABLE XLVI

MISCELLANEOUS N-SUBSTITUTED 2-OXAZOLIDONES

Empirical formula[a]	R_1	R_4	Mp, °C	% yield	Ref
$C_5H_8N_2O_3$	MeCONH	H	117	..	233
$C_{10}H_{10}N_3O_5ClS$	$3\text{-}H_2NSO_2\text{-}4\text{-}ClC_6H_3CONH$	H	182–183 ($MeOH\text{-}Et_2O$)	..	453
$C_{11}H_{12}N_3O_5Cl_5$	$3\text{-}H_2NSO_2\text{-}4\text{-}ClC_6H_3CONH$	Me	215–216 ($MeOH\text{-}Et_2O$)	..	453

[a] $R_2 = R_3 = R_5 = H$.

C. POLAROGRAPHY

Most, if not all, of the polarographic work has been on theN -(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 pseudoephedrine (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

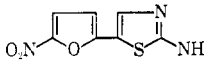
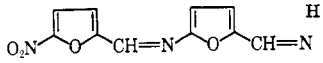
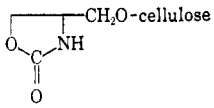
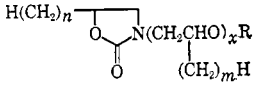
1. Furazolidone

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
$C_3H_5NO_2$	H	H	H	H	H	89–91	70	50, 462, 463
$C_3H_6N_2O_2$	H_2N	H	H	H	H	...	80	443
$C_4H_7NO_3$	H	H	H	MeO	H	...	..	463
$C_5H_5NO_2Cl$	H	$ClCH_2$	H	H	H	...	..	13
$C_7H_{10}NO_5Cl_2P$	$(MeO)_2P(O)OC(=CCl_2)$	H	H	H	H	...	..	466
$C_7H_{11}NO_2$	Me	—CH_2—		Me	Me	58–62, 98 (1)	75	132
$C_7H_{11}NO_4$	$MeCOO(CH_2)_2$	H	H	H	H	52–54 (hexane–Et_2O)	95	299
$C_8H_7N_3O_5$	5-Nitro-2-furfurylideneamino	H	H	H	H	254–255 ($MeNO_2$)	83	247, 346, 373
$C_8H_9N_3O_3$	5-Amino-2-furfurylideneamino	H	H	H	H	...	30	153
$C_8H_{12}NO_2Cl$	$ClCH_2CH_2$	—CH_2—		Me	Me	64–68	..	132
$C_9H_{10}N_2O_4S$	p-$H_2NC_6H_4SO_2$	H	H	H	H	...	..	272
$C_9H_{13}NO_2Cl_2$	i-Pr	—CCl_2—		Me	Me	44–46, 96–98 (1.8)	..	132
$C_9H_{14}NO_4SP$	$(EtO)_2P(S)CH_2CH_2$	H	H	H	H	188–192 (0.005)	..	102
$C_9H_{14}NO_5Cl_2P$	$(EtO)_2P(O)C(=CCl_2)$	H	H	H	H	...	..	446
$C_9H_{15}NO_2$	i-Pr	—CH_2—		Me	Me	87–91	..	132
$C_{10}H_8N_4O_4S$		H	H	H	H	173 (EtOH)	..	150
$C_{10}H_{10}NO_3Cl$	H	H	H	o-$ClC_6H_4OCH_2$	H	...	..	13
$C_{10}H_{10}NO_3Br$	H	H	H	p-$BrC_6H_4OCH_2$	H	151–152.5	..	13
$C_{10}H_{11}NO_3$	H	H	H	$PhOCH_2$	H	120–121	..	13
$C_{10}H_{15}NO_2$	Me	—CH_2—		—$(CH_2)_5$—		76–78	..	132
$C_{10}H_{15}NO_2Cl_2$	Bu	—CCl_2—		Me	Me	32–38, 118–120 (1)	..	132
$C_{10}H_{17}NO_2$	Bu	—CH_2—		Me	Me	112–114 (1)	..	132
$C_{10}H_{19}NO_2S$	$CH_3(CH_2)_4SCH_2CH_2$	H	H	H	H	134–136 (0.1)	96	239
$C_{11}H_{12}NO_3Cl$	H	H	H	o-$ClC_6H_4OCH_2$	Me	135–137	..	13
$C_{11}H_{13}NO_3$	H	H	H	o-$MeC_6H_4OCH_2$	H	120–122	..	13
	H	H	H	$PhOCH_2$	Me	112.5–114	..	13
$C_{11}H_{13}NO_4$	H	H	H	m-$MeOC_6H_4OCH_2$	H	121–123	..	13
	H	H	H	p-$MeOC_6H_4OCH_2$	H	103.5	..	13
	H	H	H	o-$MeOC_6H_4OCH_2$	H	139–141	..	13
$C_{11}H_{13}NO_5S$	H	p-$MeC_6H_4SO_2OCH_2$	H	H	H	...	..	13
$C_{11}H_{15}NO_2Cl_2$	Bu	—CCl_2—		Et	Me	117–119 (0.6)	..	132
$C_{12}H_{12}NO_3Cl_3$	2,4,5-$Cl_3C_6H_2OCH_2CH_2$	H	H	Me	H	76–79	13	239
$C_{12}H_{13}NO_3Cl_2$	2,4-$Cl_2C_6H_3OCH_2CH_2$	H	H	Me	H	200 (0.1)	60	239
	3,4-$Cl_2C_6H_3OCH_2CH_2$	H	H	Me	H	188–208 (0.3)	31	239
$C_{12}H_{14}NO_2ClS$	p-$ClC_6H_4SCH_2CH_2$	H	H	Me	H	...	96	239
$C_{12}H_{15}NO_3$	$PhOCH_2CH_2$	H	H	Me	H	...	50	239
	H	H	H	o-$MeC_6H_4OCH_2$	Me	99–101	..	13
$C_{12}H_{15}NO_4$	H	H	H	o-$MeOC_6H_4OCH_2$	Me	88–90	..	13
	Me	H	H	o-$MeOC_6H_4OCH_2$	H	72.5–75.0	..	13
$C_{12}H_{15}NO_5S$	H	p-$MeC_6H_4SO_2OCH_2$	Me	H	H	...	..	13
$C_{12}H_{17}NO_2Cl_2$	i-Pr	—CCl_2—		—$(CH_2)_5$—		155–157	..	132
$C_{13}H_{10}NO_6$		H	H	H	H	>300	..	152
$C_{13}H_{17}NO_3$	H	H	H	p-i-$PrC_6H_4OCH_2$	H	120–122	..	13
$C_{13}H_{17}NO_4$	Et	H	H	o-$MeOC_6H_4OCH_2$	H	175–178 (0.1)	..	13
	H	H	H	o-$MeOC_6H_4OCH_2$	Et	...	..	13
$C_{13}H_{17}NO_5S$	H	p-$MeC_6H_4SO_2OCH_2$	Et	H	H	...	..	13
$C_{16}H_{20}N_2O_4$	$Me_2N(CH_2)_3OCO$	Me	H	Ph	H	(*dl-cis*) 54	..	303
						(*dl-trans*, HCl salt) 167	..	303
$C_{17}H_{22}N_2O_4$	$Me_2N(CH_2)_3OCO$	Me	H	Ph	H	(*dl-cis*, HCl salt) 151	..	303
$C_{18}H_{19}NO_4$	$PhCH_2$	H	H	o-$MeOC_6H_4OCH_2$	H	57–58	..	13
$C_{18}H_{33}NO_2S$	$CH_3(CH_2)_4SCH_2CH_2$	H	H	Me	H	180–200 (0.1)	84	239
	Structure or name							
								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), trichonomas 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 meleagrides* (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*-methoxyphenoxymethyl)-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 antibacterial (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), antianthelmintic (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 promotors (53, 207, 408), as skeletal muscle relaxants (318, 322, 323, 350), as hypotensives (155), and as effective against organisms causing enteriocolitus (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), nematicides (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).

ACKNOWLEDGMENT.—Martin E. Dyen was supported partially under a Training Grant Award 520-831 from the National Aeronautics and Space Administration. This work was also supported in part by Public Health Service Research Grants No. CA-07803 and CA-07174 of the National Cancer Institute.

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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.

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