oxymethyl-3-phenyloxazolidin-2-one (I), m.p. 134.5–136.5°, infrared band at 5.75μ.

Anal. Calcd. for $C_{16}H_{15}NO_3$: N, 5.20. Found: N, 5.38.

Hydrolysis of the oxazolidinone I. A mixture of 23.4 g. (0.087 mole) of the oxazolidinone I, 20 g. (0.3 mole) of potassium hydroxide, 90 ml. of water, and 200 ml. of methanol was heated in a pressure bottle at 107° for 16 hr. Methanol was removed by distillation and the aqueous distillation residue was extracted with two 100-ml. portions of a 1:1 mixture of toluene and methylene chloride. The organic extract was combined with 250 ml. of 5% hydrochloric acid and the resultant mixture was steam distilled until all solvents had been removed. The clear aqueous residue was made basic by the addition of concentrated aqueous sodium hydroxide solution, whereupon an oil separated. Upon standing, the separated oil solidified and was recrystallized from a toluene/ligroin mixture to provide 16 g. (67%) of amino alcohol II, m.p. 61–62.5°, undepressed on admixture with a sample of the product from the reaction of aniline with phenyl glycidyl ether, infrared band at 3.05μ, shoulder at 3.10–3.15μ.

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.0; H, 7.0; N, 5.75. Found: C, 74.30; H, 7.24; N, 5.62.

The aqueous solution remaining after the extraction of the methanol-free reaction mixture was found to contain 0.0835 mole of carbonate ion (96%).

Amino alcohol II *from the reaction of aniline with phenyl glycidyl ether.* To 0.62 mole of redistilled aniline, held at 123–137°, was added 0.3 mole of redistilled phenyl glycidyl ether over a period of 90 min. Heating was continued for 15 min. longer after which the reaction mixture was distilled at 10 mm. to yield 0.33 mole of unchanged aniline. The pressure was then reduced and 56.2 g. of a viscous oil, b.p. 168–181° (0.05 mm.), was distilled. The oil was dissolved in a toluene/ligroin mixture and upon cooling, 53.8 g. (74%) of amino alcohol II crystallized, m.p. 61–63°.

Oxazolidinone I *from amino alcohol* II *and phosgene.* Phosgene was passed into a solution of 7.4 g. (0.03 mole) of amino alcohol II and 4.74 g. (0.06 mole) of dry pyridine in 100 ml. of methylene chloride until 0.030 mole had been absorbed. The temperature of the mixture was held at 25–30° during the addition. After standing for 24 hr., the solution was combined with 100 ml. of water and the methylene chloride was removed by distillation. The crude solid product (7 g.) was filtered, taken up in hot toluene, and clarified with Norite. Upon cooling, 4.0 g. (49%) of the oxazolidinone I crystallized, m.p. 133.5–135.5°, undepressed upon admixture with a sample of I that was prepared by the reaction of phenyl glycidyl ether with phenyl isocyanate.

Triphenyl isocyanurate (III). A mixture of 16.55 g. of phenyl isocyanate, 0.5 g. of phenyl glycidyl ether, and 0.1 g. of benzyldimethylamine was heated at 150° in a sealed tube for 2 hr. The solidified reaction mass was recrystallized from acetone to yield 15.4 g. (93%) of triphenyl isocyanurate (III), m.p. 275–277° (lit.[5] m.p. 280–281°), melting point undepressed on admixture with a sample of III prepared by the method of Hofmann,[6] infrared bands at 5.85 and 7.1μ.

Separate experiments established that none of the trimer III is formed when either phenyl glycidyl ether or benzyldimethylamine is omitted from the mixture of reactants.

Short time reaction of phenyl glycidyl ether with phenyl isocyanate. A mixture of 12.25 g. (0.103 mole) of phenyl isocyanate, 15.5 g. (0.103 mole) of redistilled phenyl glycidyl ether, and 0.1 g. of benzyldimethylamine was heated in a sealed tube at 165–170° for 90 min. The reaction mass, a semisolid sludge, was taken up in hot benzene and ligroin. Upon cooling, an impure solid (10.9 g.) separated which was resolved into two fractions by fractional crystallization. The first (5.6 g., 19%) proved to be the oxazolidinone I as evidenced by its melting point and mixed melting point with an authentic sample of I. The second product, similarly identified, proved to be the trimer III.

Oxazolidinone I *from the reaction of phenyl glycidyl ether with* III. The trimer III was prepared from the amine-epoxide catalyzed trimerization of phenyl isocyanate and melted at 276–278°. A mixture of 4.2 g. (0.0118 mole) of III, 5.4 g. (0.036 mole) of redistilled phenyl glycidyl ether, and 0.05 g. of benzyldimethylamine was heated in a sealed tube at 160° for 16 hr. The semisolid reaction mass was recrystallized from acetone to yield 3.73 g. (40%) of the oxazolidinone I, m.p. 135–137.5°, undepressed on admixture with an authentic sample of I.

n-Butylphenylurethan from the reaction of III *with n-butyl alcohol.* A mixture of 2.38 g. (0.0067 mole) of III, 1.48 g. (0.02 mole) of dry *n*-butyl alcohol, 0.03 g. of benzyldimethylamine, and 0.06 g. of phenyl glycidyl ether was heated in a sealed tube at 150° for 2 hr. The reaction mixture was taken up in hot ligroin and upon cooling, a 73% yield of impure *n*-butylphenylurethane crystallized, m.p. 54.5–58°. After repeated recrystallizations from ligroin, the melting point was raised to 59–61°, undepressed on admixture with an authentic sample prepared from the benzyldimethylamine-catalyzed reaction of *n*-butyl alcohol with phenyl isocyanate at room temperature.

Parallel experiments were carried out in which first the benzyldimethylamine and then the phenyl glycidyl ether were omitted. In either case, no urethan was formed.

5-Benzyl-3-phenyloxazolidin-2-one (IV). A mixture of 26.8 g. (0.2 mole) of redistilled benzylethylene oxide, 23.8 g. (0.2 mole) of phenyl isocyanate, and 0.2 g. of benzyldimethylamine was heated in a sealed tube at 170° for 20 hr. The reaction mixture was then heated at 110° (0.1 mm.) and 13.4 g. of distillate was collected. The latter was redistilled to provide 12 g. of unchanged benzylethylene oxide, b.p. 88–90° (8.5 mm.), $n_D^{24.5}$ 1.5194. The stripped reaction mass was taken up in hot benzene and 9.28 g. of insoluble solids were separated which yielded, after recrystallization from acetone, 8.65 g. (36.5%) of the trimer III, m.p. 277–279°, undepressed on admixture with authentic III. The benzene solution of the residual reaction produts was distilled *in vacuo* to leave a gum. The latter was recrystallized several times from a 1:1 mixture of benzene and ligroin to give 6.0 g. (12%) of 5-benzyl-3-phenyloxazolidin-2-one, m.p. 90.5–93°, infrared band at 5.76μ.

Anal. Calcd. for $C_{16}H_{15}NO_2$: N, 5.53. Found: N, 5.62.

In a second experiment, a mixture of 11.1 g. (0.093 mole) of phenyl isocyanate, 12.6 g. (0.094 mole) of redistilled benzylethylene oxide, and 0.1 g. of benzyldimethylamine was heated in a sealed tube at 160° for 69 hr. The reaction mixture was worked up as in the 20 hr. reaction to provide a 33.6% yield of the oxazolidinone IV, m.p. 90–93°. A recovery of 6% of unchanged benzylethylene oxide was realized. None of the trimer III could be isolated.

Acknowledgment. The author is indebted to D. L. Harms for the infrared spectral determinations.

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(5) I. C. Kogon, Symposium on Isocyanate Polymers, 130th Meeting, American Chemical Society, Atlantic City, N. J., September 1956, p. 62.

(6) A. W. Hofmann, *Ber.*, 18, 764 (1886).

Evidence for the Existence of Azidoximes

F. ELOY

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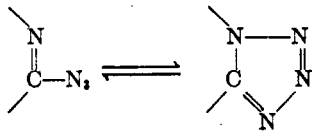
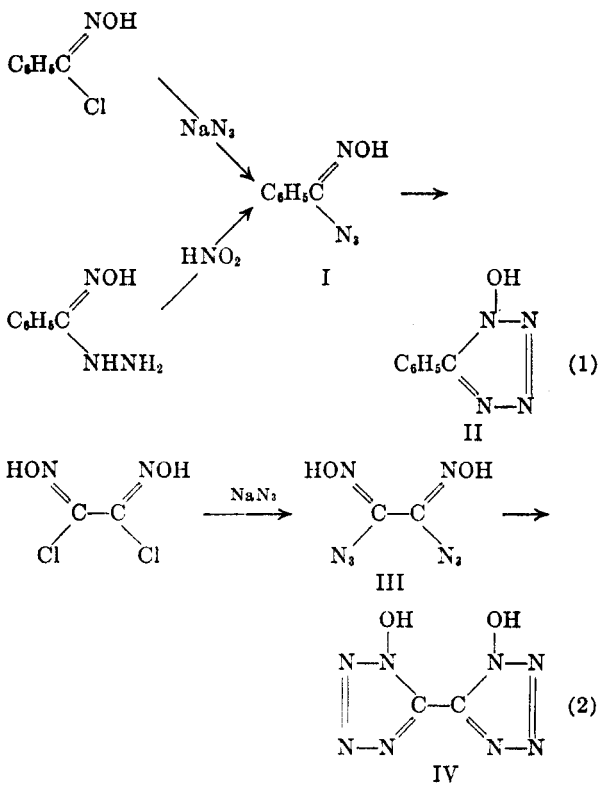
It has been suggested[1] that linear systems containing azido-azomethine groups irreversibly isom-

erize to tetrazoles. If the azomethine group is part of a heterocyclic ring, there is no general rule as to whether the compound is an azide or a tetrazole and recently[2,3] systems having the two forms in equilibrium have been discovered:



Work in this laboratory has recently revealed some significant exceptions to the above generalization for linear systems[4a]; materials described as *N*-hydroxytetrazoles have been shown to be, in fact, reasonably stable azidoximes (azides of hydroximic acids, $RC(NOH)N_3$).

As attempts to prepare azidoximes[7,8] according to reaction scheme (1) led to products not having the properties usually expected of azides, it has generally been concluded that these azidoximes, if formed, immediately isomerize to the corresponding *N*-hydroxytetrazoles.



(1) J. H. Boyer and F. C. Canter, *Chem. Rev.*, **54**, 1 (1954).

(2) J. H. Boyer and E. J. Miller, *J. Am. Chem. Soc.*, **81**, 4671 (1959).

(3) J. H. Boyer and H. W. Hyde, *J. Org. Chem.*, **25**, 458 (1960).

(4a) Other exceptions are azide derivatives of aminoguanidine and 4-phenylthiosemicarbazide.[4b, 5, 6] (b) A. Hantzsch and A. Vagt, *Ann.*, **314**, 339 (1901).

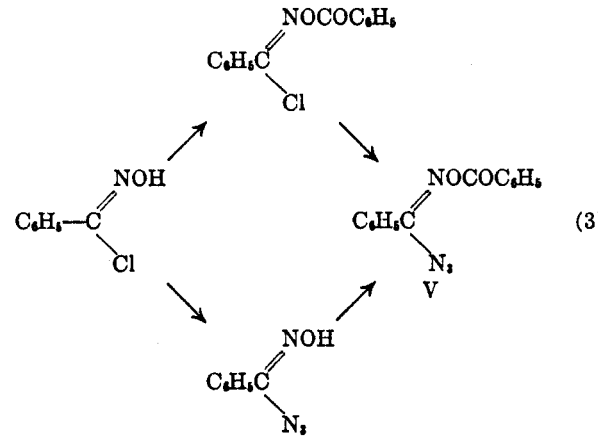
(5) M. Freund, and H. Hempel, *Ber.*, **28**, 78 (1895).

(6) H. Kovacs Nagy, A. J. Tomson, and J. P. Horwitz, *J. Am. Chem. Soc.*, **82**, 1609 (1960).

(7) M. O. Forster, *J. Chem. Soc.*, **95**, 184 (1909).

As a result, there is substantially no reference in the literature to azidoximes but only to the tetrazoles.[9-11]

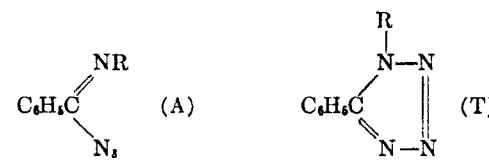
Repetition of the experiments of Forster[7] and Wieland[8] gave products with properties as described by these authors but possessing the infrared absorption band at 4.67 μ characteristic of an azide group. This band was also found in the benzoylated derivative V prepared in two separate ways:



Furthermore the published infrared spectra of a large number of tetrazoles show no band at 4.67 μ unless an azide group is present in addition to the tetrazole ring.[2,3,6,12,13]

It is believed that these facts suffice to justify assignment of the azidoxime structures I and III to the compounds which have been referred to as being II and IV, respectively. In neither case could the compound be isomerized to the corresponding tetrazole although progressive heating in common solvents led to decomposition.

In order to generalize these results a number of materials reported to be tetrazoles were synthesized[14] using the two classical reactions (1), and their spectra examined. The nature of the group R was found to determine whether a given compound exists in the azide form (A) or in the tetrazole form (T):



(8) H. Wieland, *Ber.*, **42**, 4199 (1909).

(9) V. Grignard, *Traité de chimie organique*, Masson 1953, T. XXI, p. 1071.

(10) E. H. Rodd, *Chemistry of Carbon Compounds*, Elsevier, 1954–1957, Vol. III, pp. 568, 571, and Vol. IV, p. 482.

(11) F. R. Benson, *Chem. Rev.*, **41**, 43, 45 (1947).

(12) E. Lieber, D. W. Levering, and L. J. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

(13) D. B. Murphy and J. P. Picard, *J. Org. Chem.*, **19**, 1810 (1954).

(14) With the valuable technical aid of Mr. J. Pierard.

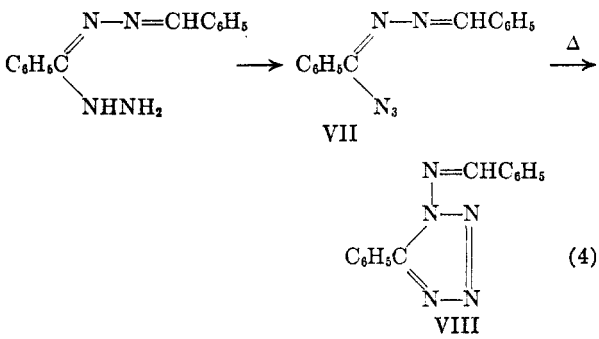
The following table summarizes the conclusions from this study.

TABLE I

R	Ref.	Structure of the Stable Product
H	[a]	T
C_6H_5	[b]	T
CH_3	[c]	T
OH[d]	[e,f]	A
OCH_3	[g]	A
$OCOC_6H_5$	[e]	A
$-N{=}CHC_6H_5$	[h,i]	A → T

[a] A. Pinner, *Ber*, **27**, 984 (1894).
[b] G. Schroeter, *Ber.*, **42**, 3356 (1909).
[c] J. v. Braun and W. Rudolph, *Ber.*, **74**, 264 (1941).
[d] The azide structure could also be confirmed in oxazidoxime (III).
[e] See ref. 7. [f] See ref. 8.
[g] Prepared from phenylazidoxime with diazomethane.
[h] R. Stollé and E. Helwerth, *Ber.*, **47**, 1132 (1914).
[i] R. Stollé and A. Netz, *Ber.*, **55**, 1297 (1922).

In all cases, except the last one, only the indicated structure is stable; Stollé[15,16] had already shown that when R = $-N=CHC_6H_5$, a stable azide (VII) could be formed which on heating in a neutral solvent isomerizes to the tetrazole (VIII):



(4)

No such isomerization occurs with azidoximes or their *O*-substituted derivatives.

Azidoximes are in fact surprisingly stable. Although they may be detonated, they can be recrystallized from boiling alcohol and several can be heated to 200° before exploding. This stability is doubtless linked to the electron donating power of the R group.

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(15) See footnote *h*, Table I.
(16) See footnote *i*, Table I.

Quinoxalines. II. Basic Ethers from 2-Chloroquinoxaline[1,2]

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The pharmacological activity of many aromatic and heteroaromatic compounds which have a tertiary amine function in a side chain linked through an ether, ester, or amide linkage prompted the synthesis of this series of quinoxaline ethers and their salts.

2-Chloroquinoxaline was allowed to react with the sodio derivative of the tertiary amino alcohol in anhydrous benzene solution. The yields of the ethers after purification by distillation under reduced pressure are high. These yields are somewhat higher than the corresponding 4-cinnoline ethers.[4] It seems likely that this is due to the greater stability of 2-chloroquinoxaline under the conditions of the reaction.

The ethers and their salts which were prepared are listed in Table I.

The pharmacological testing was performed in the Smith Kline and French Laboratories. Compounds II, III, IV, V and IX were found to be inactive in the Plasma Cholesterol Lowering Test. Compounds III, V, and IX were found to be inactive as diuretics. Compounds IV and IX were found to possess slight central nervous system depression in rats. Compounds II, III, V, VI, and IX all produced more than 93% inhibition of cholesterol biosynthesis at a concentration of $10^{-3}M$. Compound IV produced a 37% inhibition at a concentration of $10^{-3}M$. All inhibitions dropped to less than 11% at a concentration of $10^{-5}M$ except Compound VI which exhibited a 49% inhibition at this concentration. Screening data on the other compounds are not yet available.

EXPERIMENTAL[5]

2-Chloroquinoxaline. The procedure of Gowenlock, Newbold, and Spring[6] was improved by using a mixture of phosphorus oxychloride and phosphorus pentachloride. A mixture of 17 g. of 2-hydroxyquinoxaline, 23 g. of phosphorus pentachloride, and 34 ml. of phosphorus oxychloride was

(1) For Paper I in this series see R. N. Castle, A. Aldous, and C. Moore, *J. Org. Chem.*, **21**, 139 (1956).
(2) The authors are grateful to Dr. S. Yamada and to Dr. K. Abe of the Tanabe Seiyaku Co., Ltd., Tokyo, Japan for the carbon, hydrogen, and nitrogen analyses.
(3) Smith Kline and French Laboratories Post-doctoral Research Fellow, 1958–60. Present address: Tokyo Research Laboratory, Tanabe Seiyaku Co., Ltd., Toda-Cho, Saitama-Ken, Japan.
(4) R. N. Castle and M. Onda, unpublished data.
(5) All melting points are uncorrected. The infrared spectra of all of the free bases were determined on a Perkin-Elmer Infracord.
(6) A. H. Gowenlock, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 622 (1945).