ture overnight. The solution was poured through a column of neutral alumina and then evaporated on the rotovac. The resulting material was crystallized from methanol affording yellowish needles of 9: 316 mg (70.6%); mp 122.5° (lit.[5] mp 124°). The infrared spectrum indicated the presence of a carbonyl at 1764 cm$^{-1}$.

*Anal.* Calcd for $C_{14}H_9O_2N$: C, 75.34; H, 4.08. Found: C, 74.55; H, 4.04.

Hydrolysis of 120 mg of 9 in 15 ml of boiling 5% sodium hydroxide gave 105 mg of N-benzoylanthranilic acid, mp 181–181.5° (lit.[12] mp 182°).

**Sodium Borohydride Reduction of 9 to 11.**—To a solution of 300 mg of 9 in absolute ethanol was added 210 mg of sodium borohydride (excess), and the reaction mixture was allowed to sit 4 hr. The solution was evaporated to dryness in a vacuum, and the residue was extracted with hot chloroform. The chloroform solution was concentrated and cooled to yield brownish white crystals. After two recrystallizations from chloroform, 275 mg (90%) of 11, mp 175°, was obtained (ir, 1661 (C=O), 1245, and 1235 cm$^{-1}$) identical in every respect with authentic N-benzylanthranilic acid.[18]

**Registry No.**—1a, 2989-63-1; 7b, 16355-10-5; 9 1022-46-4.

**Acknowledgment.**—This investigation was supported by Public Health Service Grant CA-04474 from the National Cancer Institute.

(18) G. Lockemann and H. Rein, *Chem. Ber.*, **80**, 485 (1947).

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# Dichloro(O,O′-1,4-dioxane)zinc(II)

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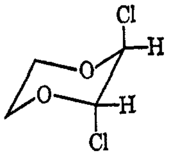
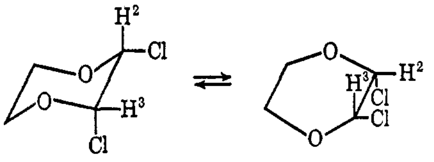
The reaction between 1,4-dioxane and chlorine produces a mixture of isomers of 2,3-dichloro-1,4-dioxane,[2] mp 30° (*trans*) and 51° (*cis*).[3,4] The *trans* isomer exists in a diaxial chair conformation [I ($C_{aa}$)] while the *cis* isomer exists in an axial–equatorial chair conformation which is continuously inverting [II ($C_{ae}$), II ($C_{ea}$)].[5–7]



I($C_{aa}$)



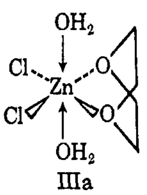
II($C_{ae}$) II($C_{ea}$)

Because *cis*- and *trans*-2,3-dichloro-1,4-dioxane constitute a valuable heterocyclic system with which to study axial/equatorial stereospecificity thresholds with respect to alkoxy substituents, it was desirable to develop a specific method for the synthesis of each isomer.

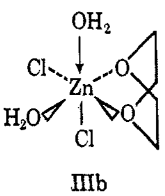
Preparation of pure I poses no problem since it is lower boiling and more thermodynamically stable than II. Preparation and isolation of pure II is more difficult owing to its ease of interconversion to I. The only method of preparing pure II reported in the literature[5] is low temperature (below 90°) chlorination of dioxane with subsequent vapor–liquid chromatographic separation of the two isomers.

The only catalyst reported used in the chlorination of 1,4-dioxane is $SnCl_2$.[8] The presence of $SnCl_2$ increased the 2,3-dichloro product yield by 28%; no product isomer distribution was reported. It was decided to try other metal chlorides (Lewis acids) but with electron configurations about the metal ion different from the $3d^{10}4s^2$ structure of $Sn^{+2}$, preferably those with vacant 4s orbitals. An added restriction was the solubility of the metal chlorides in dioxane. The metal chlorides most readily available and which meet these requirements are $ZnCl_2$, $CuCl_2$, $FeCl_3$, and $AlCl_3$. Zinc chloride, the first catalyst to be tried, selectively catalyzed the formation of II without detectable amounts of I. An investigation was then made of the structure of the zinc chloride–dioxane complex initially formed which apparently is the stereospecific catalyst for the formation of *cis*-2,3-dichloro-1,4-dioxane.

A white zinc chloride–dioxane complex has been reported as being polymeric units of $(ZnCl_2\text{–dioxane})_n$ formed at ambient temperature with the dioxane ring in the chair conformation.[9,10] The infrared spectrum of the yellow zinc chloride–dioxane complex obtained in the present study shows an increased number of absorption frequencies in the regions 2950–2870, 1960–1480, 1440–1375, and 1325–1280 cm.$^{-1}$ as compared with the dioxane chair absorption frequencies. This suggests that the complexed dioxane ring exists in a boat conformation.[9] An absorption at 620 cm$^{-1}$, indicative of oxygen–zinc bonds, also supports the dioxane boat structure with zinc chelation as the stabilizing force for the less stable boat conformation.[11] The very pronounced hygroscopic property of the complex is considered as d-orbital participation which expands the coordination number of zinc from four to six, using the $4d_{z^2}$ and $4d_{x^2-y^2}$ orbitals.



IIIa



IIIb

Although the nmr spectrum resolution of the complex in aqueous solution was insufficient to discern structure IIIa from IIIb, the respective absorption peak area ratios are sufficiently accurate to exclude the possibility of a second dioxane ring participation.

It is concluded that the structure of the zinc chloride–dioxane complex which catalyzes the stereospecific

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(1) School of Science, The University of Texas at El Paso, El Paso, Tex.

(2) J. Boseken, F. Tellegen, and P. C. Henriquez, *J. Amer. Chem. Soc.*, **55**, 1284 (1933).

(3) W. Baker and A. Shannon, *J. Chem. Soc.*, 1598 (1933).

(4) R. K. Summerbell and H. E. Lunk, *J. Amer. Chem. Soc.*, **79**, 4802 (1957).

(5) C. Altona, "Molecular Structures and Conformation of some Halogeno-1,4-dioxanes," Druco Drukkerjbedrijven, Leiden, 1964.

(6) C. Altona and C. Romers, *Acta Crystallogr.*, **16**, 1225 (1963).

(7) R. R. Fraser and C. Reyes-Zamora, *Can. J. Chem.*, **43**, 3445 (1965).

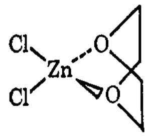
(8) J. J. Kucera and D. C. Carpenter, *J. Amer. Chem. Soc.*, **57**, 2346 (1935).

(9) P. J. Hendra and D. B. Powell, *J. Chem. Soc.*, 5105 (1960).

(10) R. Juhasz and L. F. Yntema, *J. Amer. Chem. Soc.*, **62**, 3522 (1940).

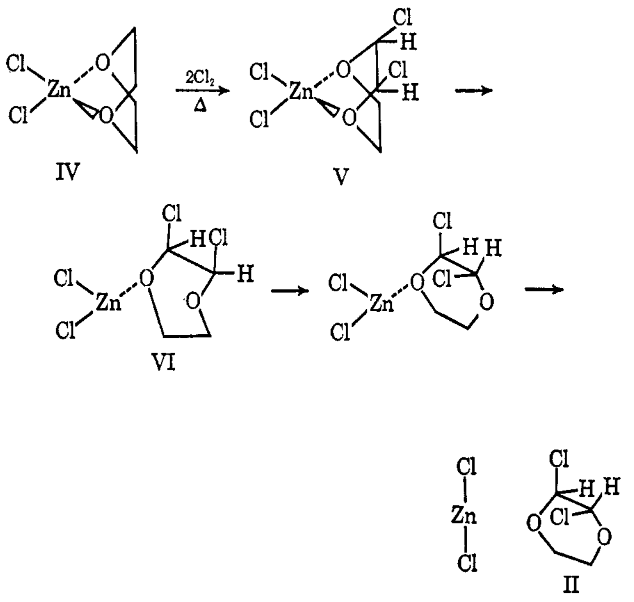
(11) K. Nakamoto, "Infrared Spectra of Inorganic and Coordination Compounds," John Wiley & Sons, Inc., New York, N. Y., pp 106 and 211.

dichloro substitution of 1,4-dioxane is dichloro(0,0′-1,4-dioxane)zinc(II).



IV

With the dioxane ring rigidly held in the boat conformation, chlorination of that ring yields the less sterically hindered *cis*-2,3-diequatorial product. The breaking of one of the chelate bonds produces the free dioxane conformer (VI). This boat to chair interconversion redefined the isomer as *cis*-2,3-axial, equatorial. Upon breaking of the second chelate bond the products are zinc chloride and *cis*-2,3-dichloro-1,4-dioxane.



### Experimental Section

***cis*-2,3-Dichloro-1,4-dioxane.**—Dioxane (800 ml, 9.40 mol) was heated to reflux under nitrogen and 64 g of anhydrous zinc chloride was quickly added. After the zinc chloride dissolved, chlorine gas was added for a 5-hr period during each of 5 days. Vapor–liquid chromatographic analysis indicated a continuous increase in production of *cis*-2,3-dichloro-1,4-dioxane with time and there was no indication of *trans* isomer formation. Distillation of the reaction mixture at 3.0 mm gave a 30% yield of the *cis* isomer, bp 55.0 ± 0.05°. The nmr spectrum of this material was essentially identical with the spectrum reported in the literature.[5]

**Dichloro(0,0′-1,4-dioxane)zinc(II).**—Anhydrous zinc chloride (3.44 g) was added to 120 ml of dioxane distilled over lithium aluminum hydride. The mixture was heated for 48 hr at 90°. When the yellow reaction mixture was cooled to ambient temperature, yellow crystals formed. Additional crystals were obtained by the addition of cyclohexane. The total yield was 6.08 g. The dry, very hygroscopic, crystals decomposed at 160°.

*Anal.* Calcd for $C_4H_8O_2Cl_2Zn$: C, 21.43; H, 3.60; Cl, 31.6. Found:[12] C, 21.11; H, 3.86; Cl, 30.8.

Gravimetric chloride ion determination indicated 1.96 ± 0.01 mol of $Cl^-$/mol of complex.

The infrared spectrum was obtained in potassium bromide pellets (30% concentration). The nmr spectrum was made on a 50% solution in water. This solution had the same color as the complex. There was a broad absorption band at $\tau$ 1.07 downfield from the water proton absorption with respective integration ratios of 12 and 2.

**Registry No.**—IV, 16457-66-2.

**Acknowledgment.**—This research was supported by a grant from the Robert A. Welch Foundation.

## Synthesis of 4-Oxoglutaraldehydic Acid Derivatives from Nitrofurans and Aminofurans

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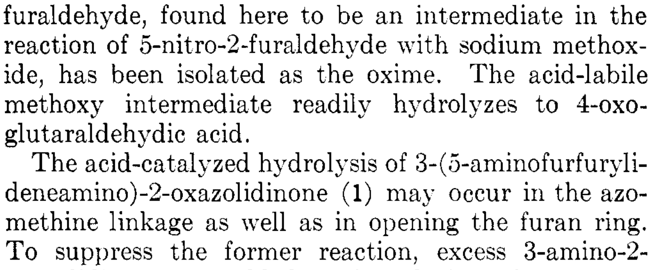
Certain nitrofurans are reduced both chemically[1] and biologically[2] to the corresponding aminofurans. Biologically, $^{14}C$ is found in metabolites, including glutamic acid, when $^{14}C$-labeled nitrofurans are fed to chickens. Alkaline hydrolysis of ethyl 5-amino-2-furoate has also been reported; α-ketoglutaric acid was identified.[3] These observations suggested conversion of the five-carbon furaldehyde moiety into glutamic acid *via* α-ketoglutaric acid[4] and led to this study of the hydrolytic ring opening of nitrofurans and aminofurans.

In this note we reported the isolation of 4-oxoglutaraldehydic acid as a 3-amino-2-oxazolidinone derivative from the acid hydrolysis of 3-(5-aminofurfurylideneamino)-2-oxazolidinone and as a bissemicarbazone from the reaction of 5-nitro-2-furaldehyde dimethyl acetal with sodium methoxide. For comparison, 4-oxoglutaraldehydic acid was synthesized from 3,5-dibromolevulinic acid as described by Wolff[5] and the same derivatives were isolated. In addition, 5-methoxy-2-furaldehyde, found here to be an intermediate in the reaction of 5-nitro-2-furaldehyde with sodium methoxide, has been isolated as the oxime. The acid-labile methoxy intermediate readily hydrolyzes to 4-oxoglutaraldehydic acid.

The acid-catalyzed hydrolysis of 3-(5-aminofurfurylideneamino)-2-oxazolidinone (1) may occur in the azomethine linkage as well as in opening the furan ring. To suppress the former reaction, excess 3-amino-2-oxazolidinone was added to the solution of reactants. The isolated product, 5-(2 oxo-3-oxazolidylimino)-levulinic acid (2), was identical with the authentic compound.



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[12] Analysis by Clark Microanalytical Laboratory which reported ". . . .frankly, this is the most hygroscopic material which we have ever seen."

[1] F. F. Ebetino, J. J. Carroll, and G. Gever, *J. Med. Pharm. Chem.*, **5**, 513 (1962).

[2] J. Olivard, S. Valenti, and J. A. Buzard, *ibid.* **5**, 524 (1962).

[3] G. M. Klein, J. P. Heotis, and J. A. Buzard, *J. Biol. Chem.*, **238**, 1625 (1963).

[4] R. J. Herrett, C. W. Williams, J. P. Heotis, and J. A. Buzard, *J. Agr. Food Chem.*, **15**, 433 (1967).

[5] L. Wolff, *Ann.*, **260**, 79 (1890).