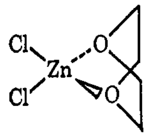
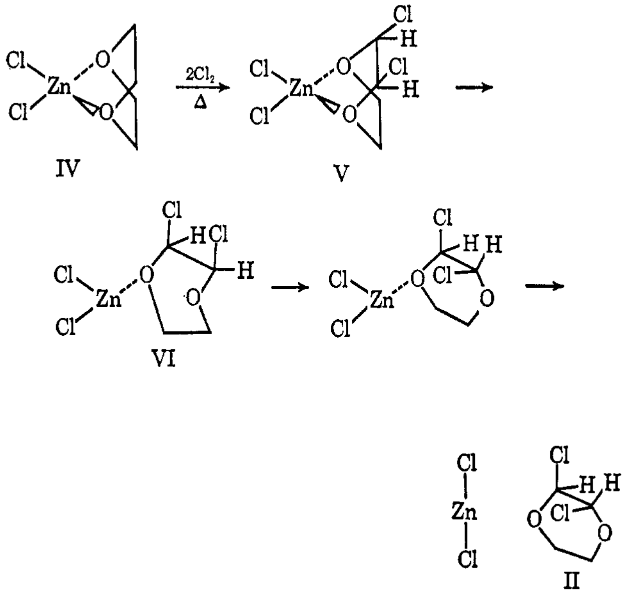
dichloro substitution of 1,4-dioxane is dichloro(0,0′-1,4-dioxane)zinc(II).



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 τ 1.07 downfield from the water proton absorption with respective integration ratios of 12 and 2.

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

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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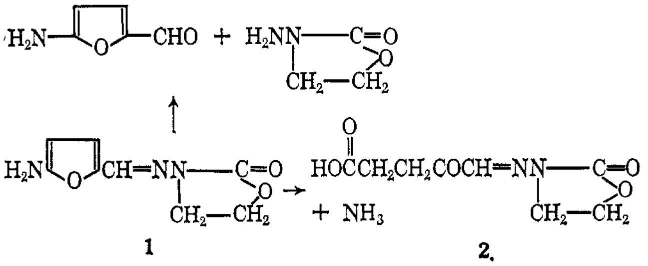
Certain nitrofurans are reduced both chemically[1] and biologically[2] to the corresponding aminofurans. Biologically, ^{14}C is found in metabolites, including glutamic acid, when ^{14}C-labeled nitrofurans are fed to chickens. Alkaline hydrolysis of ethyl 5-amino-2-furoate has also been reported; α-ketoglutaric 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.



1 2

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[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).

Under the same conditions, the hydrolytic reaction was followed spectrally. An isosbestic point at 290 mμ indicated negligible side reactions. At 70° in 2 *M* HCl with this method, the aminofuran was converted into the acid in 93% yield (spectrally) with a half-life ($t_{1/2}$) of about 5.5 min (Table I).

TABLE I

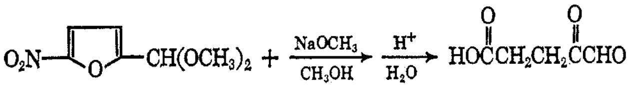
RATE OF CONVERSION OF 1 INTO 2 IN AQUEOUS ACID

Time, min	Absorbance	
	1[a]	2[b]
1	0.698	0.076
4	0.444	0.205
8	0.250	0.320
15	0.112	0.396
30	0.061	0.433

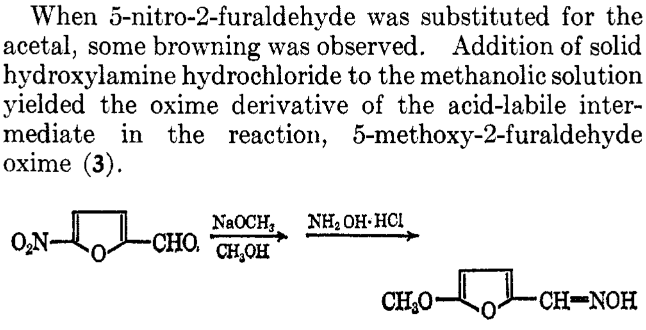
[a] uv max, 338 mμ (ε 22,300). [b] uv max, 266 mμ (ε 16,600).

To determine whether the aminofuran is hydrolyzed directly to the free acid or through an intermediate nitrile, 5-(2-oxo-3-oxazolidylimino)levulinonitrile prepared from 3,5-dibromolevulinonitrile was subjected to the exact conditions of the aminofuran hydrolysis. The nitrile group was not hydrolyzed. The infrared spectrum of the product exhibited nitrile absorption and no carbonyl group other than that of the aminooxazolidinone ring. In the extraction of the nitrile, the partition coefficient (ethyl acetate:water) was 0.8. The partition coefficient for the corresponding acid is less than 0.2. If the nitrile had been present in the aminofuran hydrolysis mixture, it should have been recovered with (or in preference to) the acid.

With aqueous sodium hydroxide and several conditions of concentration of reactants, temperature and time of reaction, synthesis of 4-oxoglutaraldehydic acid derivatives from nitrofurans was unsuccessful. Only dark brown reaction mixtures and tars were obtained. However, when 5-nitro-2-furaldehyde dimethyl acetal at molarity less than 0.15 was treated with sodium methoxide in methanol solution, the reaction went to completion with only slight browning. 4-Oxoglutaraldehydic acid was isolated from the reaction mixture as the bissemicarbazone following acid hydrolysis of the acetal group.



When 5-nitro-2-furaldehyde was substituted for the acetal, some browning was observed. Addition of solid hydroxylamine hydrochloride to the methanolic solution yielded the oxime derivative of the acid-labile intermediate in the reaction, 5-methoxy-2-furaldehyde oxime (3).



3

Measurement of the rate of reaction of nitrofurans (0.0355 *M*) with sodium methoxide (0.25 *M*) utilized acid-stable absorbance near 310 mμ. Total absorbance represents both nitrofuran reactant and 5-methoxyfuran product. Acid stable absorbance represents nitrofuran only since the 5-methoxyfurans are hydrolyzed in acid solution to 4-oxoglutaraldehydic acid which exhibits only low end absorption in the ultraviolet spectrum. The rate of decrease in acid stable absorbance, *i.e.*, rate of decrease in nitrofuran concentration, is the rate of the reaction which yields 5-methoxyfurans provided there are no side reactions. The stability of total absorbance in methanol at 310 mμ indicated no side reactions with 5-nitro-2-furaldehyde and 5-nitro-2-furaldehyde dimethyl acetal. From the acid-stable absorption spectrum of the reaction of 5-nitro-2-furaldehyde with sodium methoxide at 38°, $t_{1/2}$ = 6.6 min was calculated. Doubling the sodium methoxide concentration decreased the half-life to 4.5 min, indicating the participation of the methoxide anion in a bimolecular rate-limiting step.

The rate of reaction of 5-nitro-2-furaldehyde dimethyl acetal with sodium methoxide in methanol solution was only slightly slower than that of the aldehyde; the half-life at 38° was 10.0 min. The approximate rate of acid hydrolysis of 5-methoxy-2-furaldehyde to 4-oxoglutaraldehydic acid also was measured spectrally. The calculated half-life in 0.25 *M* HCl at 67° was 2.7 min.

Experimental Section

Acid Hydrolysis of 3-(5-Aminofurfurylideneamino)-2-oxazolidinone (1).—Compound 1[1] (0.5 g) and 3-amino-2-oxazolidinone (1.0 g) were dissolved in 150 ml of water and heated to 70° in a water bath. The solution was combined with 150 ml of 4 *M* HCl at the same temperature. After 15 min the solution was cooled, partially neutralized with 100 ml of 4 *M* NaOH and extracted four times with equal volumes of ethyl acetate. The ethyl acetate extracts were concentrated *in vacuo* to yield a brownish crystalline product in 18% yield. Recrystallization from 95% ethanol (with charcoal treatment) yielded a white crystalline acidic product, 5-(2-oxo-3-oxazolidylimino)levulinic acid (2): mp 190°; uv max (water), 266 mμ (ε 16,600); and ir (mull) C=O at 1776 and 1672 cm^{-1}. All were identical with that of the authentic compound prepared from 4-oxoglutaraldehydic acid synthesized from 3,5-dibromolevulinic acid by the method of Wolff.[5]

Anal. Calcd for $C_8H_{10}N_2O_5$: C, 44.86; H, 4.71; N, 13.08. Found: C, 44.82; H, 4.69; N, 13.13.

The acid hydrolysis rate data for the conversion of the aminofuraldehyde 1 into the oxoglutaraldehydic acid derivative 2, followed spectrally, is given in Table I.

5-(2-Oxo-3-oxazolidylimino)levulinonitrile was prepared from 3,5-dibromolevulinonitrile.[6]

4-Oxoglutaraldehydic Acid Bissemicarbazone.—In a typical experiment, 1 g of 5-nitro-2-furfuraldehyde dimethyl acetal was added to 40 ml of 0.5 *M* sodium methoxide in methanol at reflux and the heating was continued for 30 min. The solution was cooled, neutralized with carbon dioxide, and concentrated *in vacuo*, and the solids were removed by filtration. The filtrate was made acidic with 2 *M* HCl and nitrogen was bubbled through it to remove HNO_2 and CO_2. Semicarbazide hydrochloride (1.5 g) was added. After 12 hr in the refrigerator, off-white crystals were obtained; these were twice dissolved in 5% $NaHCO_3$ and reprecipitated with 2 *M* HCl added dropwise; the bissemicarbazone of 4-oxoglutaraldehydic acid was obtained in 15% yield: ir (mull) C=O at 1701 (sh), 1681 and 1575 cm^{-1}; uv max (water), 286 mμ (ε 29,700). All were identical with that of the authentic compound synthesized by an alternative route.[5]

Anal. Calcd for $C_7H_{12}N_6O_4$: C, 34.4; H, 4.95; N, 34.4. Found: C, 34.2; H, 4.81; N, 32.8.

5-Methoxy-2-furaldehyde Oxime (3).—5-Nitro-2-furaldehyde (1 g) was added to 100 ml of refluxing 0.25 *M* sodium methoxide in methanol and the reflux was continued for 10 min. Hydroxylamine hydrochloride (3.5 g) was added and the reflux was continued for 15 min. After cooling and concentration *in vacuo*, off-white crystals of 5-methoxy-2-furaldehyde oxime (3) precipi-

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(6) F. L. Austin, *Chem. Ind.* (London), 523 (1957).

tated in 45% yield. The product, recrystallized from methanol-water with charcoal treatment, was white: mp 145-146°; uv (water), 287 mμ (ε 22,600), in dilute HCl a reversible shift in uv max to 337 mμ was found; ir (mull), 2740, 1629, 1575, 1615, 1299, 1220, 1050, and 1016 cm^{-1}; nmr (DMSO), δ 3.78 (s, 3, CH_3O), 5.43 (d, 1, J = 3 Hz, CH of C4), 7.12 (d, 1, J = 3 Hz, CH of C-3), 7.2 (s, 1, CH=N), and 11.5 (s, NOH).

Anal. Calcd for $C_6H_7NO_3$: C, 51.06; H, 5.00; N, 9.93. Found: C, 50.96; H, 4.90; N, 9.78.

Kinetics of the Reaction of Nitrofurans with Sodium Methoxide.—For the determination of the rate of reaction the nitrofurans were mixed quickly with 0.25 M sodium methoxide in methanol already equilibrated at 38°. The final concentration of nitrofuran was 0.0355 M. At appropriate time intervals, two 0.5-ml aliquots were diluted (1) with methanol to determine total absorbance at 310 mμ and (2) with 4 M HCl to determine acid-stable absorbance at 310 mμ. The absorbance of the latter sample was measured after heating for 10 min in a 70° water bath. Spectra were recorded on the Beckman DB recording spectrophotometer.

Rate of Acid Hydrolysis of 5-Methoxy-2-furaldehyde.—5-Nitro-2-furaldehyde (3.55 mmol) was heated at reflux for 10 min in 100 ml of 0.25 M sodium methoxide in methanol. Without isolation of the 5-methoxy-2-furaldehyde the solution was diluted 1:10 with HCl to give a final acid concentration of 0.25 M. After appropriate intervals in a 67° water bath, aliquots were diluted with NaOH-phosphate buffer (final pH, 7.0) and the absorbance read at 310 mμ.

Registry No.—**2**, 16487-09-5; 4-oxoglutaraldehydic acid bissemicarbazone, 16487-29-9; **3**, 16487-30-2.

Acknowledgment.—Reference compounds were synthesized by Mr. Frank F. Ebetino of the Organic Chemistry Section, Eaton Laboratories. Dr. Julian Michels of the Analytical Chemistry Section, Eaton Laboratories, supplied the infrared spectra, and Dr. Jerrold Meinwald, Department of Chemistry, Cornell University, supplied the nmr spectra.

The Synthesis of Triarylalkyl Ammonium Salts[1]

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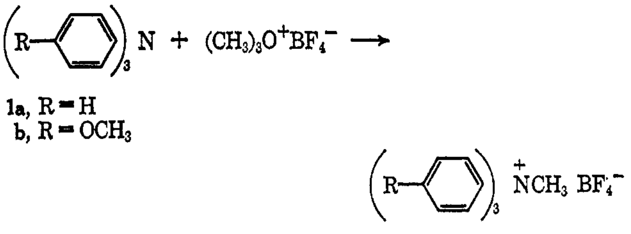
In contrast to the extensive studies of alkyl quaternary ammonium salts,[2] aryl quaternary ammonium salts have only been slightly investigated. In part, this is probably due to the marked decrease in the basic and nucleophilic properties of aryl amines making quaternization somewhat difficult. Diaryldialkylammonium salts are mentioned only rarely in the chemical literature,[3] and triarylalkylammonium salts have not yet been reported.[4] In the following, we report the synthesis of the hitherto unknown triarylalkylammonium salts.

The synthesis of triarylmethylammonium salts **2** was accomplished through alkylation of the required triarylamine with trimethyloxonium tetrafluoroborate[5] in methylene chloride at 75°. As expected, the nucleophilicity of the nitrogen atom is significantly increased by the substitution of a *para* methoxyl group **1b** and the rate of formation of **2b** is considerably greater than for **2a**.



1a, R = H
b, R = OCH_3

2a, R = H
b, R = OCH_3

Both of the triarylalkylammonium tetrafluoroborates **2** are quite stable solids. They do not appear to be appreciably hygroscopic and have shown no signs of decomposition on storage. Both salts can be held above their melting points and recovered essentially unchanged. (Some color does develop on heating, but the spectra of the recovered materials are superimposable on those of the original salts.)

In contrast to the thermal stability of these materials, they are quite labile to treatment with base. Thus, when **2a** is allowed to react with a series of basic reagents (*n*-butyl lithium–hexane or dichloromethane, *t*-butyl lithium–pentane or tetrahydrofuran, phenyl lithium–benzene–ether, potassium methoxide–methanol, potassium *t*-butoxide–dimethyl sulfoxide), demethylation occurs to yield the parent triarylamine. A similar result is observed with **2b** using *n*-butyl lithium–hexane, dichloromethane, or potassium methoxide–methanol.

Crude kinetics of demethylation by potassium methoxide in methanol-OD have been followed using nmr spectroscopy. The second order rate constants at 0° are approximately 3×10^{-5} l. mol^{-1} sec^{-1} and 7×10^{-6} l. mol^{-1} sec^{-1} for **2a** and **2b**, respectively. No hydrogen–deuterium exchange of the N-methyl hydrogen atoms was observed in these reactions.

Experimental Section

Analytical Data.—Nmr spectra were obtained using a Varian A-60 spectrometer and chemical shifts are reported as downfield from internal TMS. Infrared spectra were obtained on a Perkin-Elmer Infracord as solutions in carbon tetrachloride or chloroform. Ultraviolet spectra were obtained on a Cary spectrophotometer as a solution in absolute ethanol. Melting points were obtained on a Hoover apparatus and are corrected.

Triphenylmethylammonium Tetrafluoroborate (2a).—To 2.7 g of triphenylamine in 27 ml of dichloromethane was added 2.7 g of trimethyloxonium tetrafluoroborate.[5] The reaction vessel was degassed and sealed under vacuum. It was stirred at 75° for 22 days. The resulting blue solution was evaporated to dryness and the resulting solid successively washed with diethyl ether to yield an ether-insoluble material. Recrystallization from absolute ethanol gave 0.6 g of material with mp 182.0–183.5°. An analytical sample had mp 185.5–186.0°; nmr ($CDCl_3$), δ 4.67 (s, 3, $^+NCH_3$), 7.1–7.8 (m, 15, C_6H_5); ir ($CHCl_3$), 3.3 (m), 6.3 (s), 6.7 (s), 7.9 (s), 9.4 (v.s.), 11.0 μ (s); uv max (absolute

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(1) We gratefully acknowledge the Los Angeles State College Foundation for partial support of this work.

(2) See, for example, (a) A. C. Cope and E. R. Trumbell, *Org. Reactions*, **11**, 317 (1960); (b) H. E. Zimmerman in "Molecular Rearrangements," P. deMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 345.

(3) (a) D. A. Archer and H. Booth, *J. Chem. Soc.*, 322 (1963); (b) E. D. Hughes and D. J. Whittingham, *ibid.*, 806 (1960); (c) E. Muller, H. Huber-Emden, and W. Rundel, *Ann.*, **623**, 34 (1959).

(4) (a) P. A. S. Smith, "Chemistry of Open Chain Nitrogen Compounds," Vol. 1, W. A. Benjamin, Inc., N. Y., 1965, p 92; (b) I. T. Millar and H. D. Springall, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, London, 1966, p 162.

(5) H. Meerwein, G. Hinz, P. Hofmann, E. Kroning, and E. Pfeil, *J. Prakt. Chem.*, **147**, 257 (1937).