The Reaction of Oxalyl Chloride with Amides. I. The Preparation of Furanone Amines

A. J. SPEZIALE AND L. R. SMITH

Agricultural Research Department, Agricultural Chemicals Division, Monsanto Chemical Company, St. Louis 66, Missouri

Received July 6, 1962

The reaction of N,N-disubstituted acetamides with oxalyl chloride led to 5-disubstituted amino-2,2,4-trichloro-3(2H)furanones. Proof of the structure and the mechanism of formation is discussed. A new synthesis of trichlorovinylamines and an amide-acid bromide exchange reaction are reported.

The reaction of trichlorovinylamines^{1,2} (I) with mineral acids has been shown to yield iminium salts (IIa) **.2**

Since this reaction is reversible² and since iminium salts (11) may be viewed as a type of amido ~hloride,~ an alternate synthesis of chlorinated vinylamines by way of chloroacetamido chlorides was visualized. Amido chlorides may be prepared by the action of chlorinating agents (phosphorus pentachloride, thionyl chloride, oxalyl chloride, phosgene) on amides.³ The preparation of α chloroenamines *via* amido chlorides could perhaps also be extended to a variety of cases other than the β -dichloro case by treatment of the proper amide with a suitable chlorinating agent.

Treatment of **N,N-diethyl-2,2-dichloroacetamide** (IIIa) with phosphorus pentachloride did indeed lead to the isolation of N,N-diethyl-1,2,2-trichlorovinylamine (Ia) in 16% yield.⁴ The amido or iminium chloride (113) was not isolated.

An attempt to prepare a 1,2-dichlorovinylamine $I(Y=H)$ by this method also led to a trichlorovinylamine. Treatment of N-methyl-2-chloroacetanilide (IIIb) with phosphorus pentachloride yielded only N-methyl-N-phenyl-1,2,2-trichlorovinylamine (Ib). In this case chlorination of the amido chloride (IIb) must have occurred prior to the loss of hydrogen chloride.

(1) Prepared **by** the reaction of N,N-disubstituted 2,2,2-triehlorc acetamides with tertiary phosphines.

(2) A. J. Speziale and R. C. Freeman, *J.* Am. Chem. *Soc.,* **82, 903, ⁹⁰⁹**(lS60).

(3) H. Eilingsfeld. M. Seefelder, and H. Weidinger, *Angsur.* Chem., **72, 836 (1960).** (4) With R. C. Freeman.

Amides have been shown to undergo facile *a*chlorination⁵ on treatment with phosphorus pentachloride.

In order to avoid this α -chlorination, milder chlorinating agents were investigated. Treatment of N,N-diethyl-2-chloroacetamide with thionyl chloride led to recovery of starting material.

Treatment of N,N - diethyl - *2* - chloroacetamide with one mole of oxalyl chloride led to a 40% recovery of the starting amide and a white crystalline solid which did not have the properties expected of an amido chloride. Reaction of one mole of the amide with two moles of oxalyl chloride produced the identical material in 94% yield. Hydrogen chloride and carbon dioxide were evolved during the reaction.

The product, from the reaction of N,N-diethyl-2 chloroacetamide with oxalyl chloride, based on physical properties and hydrolysis behavior, is formulated as 5-diethylamino-2,2,4-trichloro-3 (2H) furanone (IVa).

$$
R_3CH_2-C-N
$$

\n
$$
R_1 + 2(COCI)_2 \rightarrow R_1
$$

\n
$$
R_2
$$

\n
$$
R_3
$$

\n
$$
R_1 = R_2 = C_2H_5, R_3 = Cl
$$

\n
$$
R_1 = R_2 = CH_3, R_3 = Cl
$$

\n
$$
R_1 = C_4H_5, R_2 = Cl
$$

\n
$$
R_1 = C_4H_5, R_2 = Cl
$$

\n
$$
R_1 = R_2 = CH_3, R_3 = Cl
$$

\n
$$
R_1 = R_2 = C_3H_5, R_3 = Cl
$$

\n
$$
R_1 = R_2 = C_3H_5, R_3 = Cl
$$

The reaction of acetamides with oxalyl chloride to form furanone amines has been extended to N,N - dimethyl - **2** - chloroacetamide, N - methyl-*2* - chloroacetanilide, N,N - diphenyl - *2* - chloroacetamides, and N,N-diethyl-2-phenylacetamide. the products being the furanone amines IVb-IVe.

(4) With R. C. Freeman. *(5)* J. **v.** Brsun, **F.** Jostes. and W. Munch, Ann., **463, 113 (1926).**

TABLE I **FURANONE AMINES**

^{*a*} Uncorrected. ^{*b*} Beckman IR 4. ^{*c*} Cary Model 14. d Inflection.

The physical constants of these furanone amines are given in Table I.

X,K-Diethylacetamide reacts vigorously with oxalyl chloride but no crystalline material could be isolated from the dark brown tar which was produced. **N,N-Diethyl-2,2-dichloroacetamide** did not react with oxalyl chloride under normal conditions and gave a 51% recovery of starting material under forcing conditions.

Treatment of IVa with refluxing 10% hydrochloric acid gave carbon dioxide, diethylamine (isolated as N,N-diethyl-p-toluenesulfonamide) and chloropyruvic acid (isolated as methyl chloropyruvate). The methyl chloropyruvate isolated from the hydrolysis was identical with a sample prepared by chlorination of methyl pyruvate with sulfuryl chloride **.6**

Hydrolysis of IVe under comparable conditions gave phenylpyruvic acid in **59%** yield.

The sequence, amide \rightarrow IV \rightarrow V, may constitute a convenient and preparative method for α -substituted pyruvic acids. The formation of chloroand phenylpyruric acids is consistent with struc-

(6) The presence of a strong temperature dependent hydroxyl absorption in the infrared spectrum of methyl chloropyruvate indicates that the compound exists to a significant degree in the enol form. An attempt to prepare the **2.4-dinitrophenylhydrazone** of methyl chloropyruvate in methanol led to a mixture **of** a-chloro derivative and methyl methoxypyruvate **2,4-dinitrophenylhydrazone.** Replacement of the chlorine atom by a methoxy group during the preparation of a **2,4-dinitrophenylhydrazone** of an a-chloro carbonyl compound in methanol has been reported by other workers. Methyl chloropyruvate **2,4-dinitrophenylhydrazone** waa prepared in 96% yield on treatment **of** the ester with 2.4-dinitrophenylhydrazine in 12 *N* hydrochloric acid. See: F. Ramirez and A. F. Kirby, *J. Am. Chem. Soc., 74,* 4331 (1952); **76, GO26** (1953), **A.** Ross and R. N. Ring, *J. Org. Chem.,* **26,** 679 (1961).

It is well known that enamines are easily hydrolyzed in acid media. The hydrolysis of IT' would lead to an unsymmetric diacid chloride which would he expected to hydrolyze immediately to give an α -ketodicarboxylic acid. The latter type of compound is known to decarboxylate very readily.

The ultraviolet spectra of IV are quite consistent with those reported for straight chain enamino ketones⁷ (λ_{max} 254-307 m_{μ}, log ϵ 4.11-4.51). We have prepared the cyclic enamino ketones⁸ VIa and VIb and have found ultraviolet absorption maxima at $302 \text{ m}\mu$ (log ϵ 4.54) and $305 \text{ m}\mu$ (log ϵ 4.55). respectively. These values are also in agreement with the presence of an enamino ketone system in **IT'.**

The mechanism for the formation of furanone amines by the action of oxalyl chloride on amides is visualized as proceeding *via* a sequence of reactions involving enamine and iminium structures. Undoubtedly the first step in the reaction sequence is the acylation of the amide to produce VII. Acylation could also occur *via* the amide enol but the reaction is formulated as above because the presence of phenyl groups on the amide nitrogen atom (which should reduce the nucleophilicity of the nitrogen atom but should not suppress enolization) slows the reaction. Hall⁹ has isolated addition compounds of acid bromides with dimethylformamide and has shown that they have the structure XI which is similar to the intermediate VII.

The iminium salt VI1 would be expected to lose hydrogen chloride readily to form the enamine VIII. The presence of the α -substituent *(i.e.,* chlorine or phenyl) should impart increased acidity to the α -hydrogens and facilitate their loss. The lower acidity of the α -hydrogen atoms of N,N-diethylacetamide could account for the failure of this compound to undergo the reaction.

Intramolecular C-acylation of the enamine (VIII) would yield the cyclic iminium keto lactone (IX) which again would be expected to lose hydro-

^{(7) (}a) **S. A.** Glickman and **A.** C. Cope, *J. Am. Chem. Soc., 67,* 1017 (1945); (b) **E. A.** Braude, *Ann. Rept. Progr. Chem. (Chem. SOC. London).* **42, 105** (1945); (c) **S.** Baldwin, *J. Org. Chem., 26,* **3288 (1961).** (8) N. **J.** Leonard and J. **A.** Adamcik, *J. Am. Chem.* Soc., **81, ⁵⁹⁵**

 $(1959).$ **(9) H. K.** Hall, Jr., *tbzd.,* **78,** 2717 (1933).

gen chloride readily. X then undergoes chlorination by the second mole of oxalyl chloride.

The chlorination of a carbonyl group by oxalyl chloride is a known reaction.'" The chlorination is probably facilitated by the fact that the intermediate X should be a highly strained species and the chlorination would partially relieve the strain. The formation of the stable, conjugated product would favor chlorination at the carbonyl group adjacent to the oxygen atom. The observed stoichiometry is quite consistent with this scheme.

Two moles of oxalyl chloride are required and one mole of carbon dioxide is evolved during the reaction. One mole of hydrogen chloride is also evolved during the reaction and more is liberated during the work-up.

Since the conversion of VI11 to IX involves the acylation of an enamine,¹¹ it was of interest to determine whether an alkylation could be effected in this step. For example, the reaction of N,N-diethyl-2-chloroacetamide with bromoacetyl bromide could perhaps lead to a cyclic product derived from the subsequent cyclization of the 0-acylated intermediate XII. This reaction, however, at room temperature for seventy-two hours followed by treatment with excess water led to the isolation of N,h'-diethyl-2-bromoacetamide along with some starting chloroamide. This exchange reaction probably proceeds *via* a series of equilibria involving 0-acylated and K-acylated intermediates (Chart I), Hydrolysis of the reaction mixture would yield the isolated products.

X similar exchange must take place during the formation of dimethyl amides by the reaction of acid chlorides with dimethylformamide.12

- **(11) S. Hiinig, E. Benzing. and E. Luoke,** *ibid.,* **90, 2833 (1957); 91, 129 (1958).**
	- (12) G. M. Coppinger, *J. Am. Chem. Soc.*, **76**, 1372 (1954).

The reaction goes to completion in this case since the formyl chloride formed is unstable and is lost as gaseous products.

Experimental¹³

N,N-Diethyl-l,2,2-trichlorovinylaine (Ia) **.4-A** mixture of S,N-diethyl-2,2-dichloroacetamide **(73.6** g., **0.4** mole) and phosphorus pentachloride **(83.3** g., 0.4 mole) was stirred for **48** hr. at room temperature and then for 24 hr. a **50-51'.** Fractional distillation gave a forerun, b.p. **25-75' (14** mm.), and then somewhat impure N,N-diethyl-1,2,2-trichlorovinylamine **(13.4** g., **0.066** mole, **l6Yc),** b.p. **67-75' (11-14** mm.), $n^{25}D$ 1.4865; reported² b.p. 67° (6.2 mm.), $n^{25}D$ **1.4850.** The infrared spectrum was essentially identical with that of an authentic sample.

Reaction of N-Methyl-2-chloroacetanilide and Phosphorus
Pentachloride. N-Methyl-N-phenyl 1,2,2-trichlorovinyl-N-Methyl-N-phenyl 1,2,2-trichlorovinyl $amine$ (Ib). $-A$ solution of N-methyl-2-chloroacetanilide **(16.0** g., 0.09 mole) in benzene was stirred while phosphorus pentachloride **(21.0** g., **0.1** mole) was added. The mixture was heated at *40'* for **1** hr. and benzene and phosphorus oxychloride were removed *in vacuo.* Distillation produced a small forerun and then a yellow liquid (9.0 g.), b.p. 116-129° **(3-3.5** mm.). Redistillation gave N-methyl-N-phenyl- $1,2,2$ -trichlorovinylamine $(2.6 \text{ g.}, 0.01 \text{ mole}, 11\%)$, b.p. 94-98' **(0.4-0.7** mm.), *12.2%* **1.5847;** reported b.p. 105' (0.5 mm.)¹⁴, $n^{25}D$ 1.5859.¹⁴ The infrared spectrum was identical with that of an authentic sample.¹⁴ Further distillation gave N-methyl-2-chloroacetanilide **(4.3** g., *27%),* b.p.

(14) A. J. **Speziale and** L. R. **Smith,** *J. Am. Chem. Soc.,* **84, 1868 (1962).**

⁽¹⁰⁾ H. Staudinger, *Be?.,* **42, 3966 (1909).**

⁽¹³⁾ Melting points are uncorrected.

104-122" (1 mm.) which solidified on standing. The infrared spectrum was identical to an authentic sample.

5-Diethylamino-2,2,4-trichloro-3(2H)-furanone (IVa).- **A** solution of N,N-diethyl-2-chloroacetamide (10.0 g., 0.067 mole) in methylene chloride (70 ml.) was stirred while oxalyl chloride (17.0 g., 0.135 mole) was added dropwise. The exit gases were swept into a 10% sodium hydroxide solution by a slow stream of dry nitrogen. The methylene chloride solution was stirred for 2 hr. and the sodium hydroxide solution was found to contain carbonate ion (0.04 mole.) 60% , as BaCO₃) and chloride ion (0.05 mole, 76%, by potentiometric titration).

Evaporation of the methylene chloride *in vacuo* left a fuming solid residue (19.2 g.) which on recrystallization (with charcoal) from methylene chloride-hexane gave 5 **diethylamino-2,2,4-trichloro-3(2H)-furanone** (17.0 g., 0.063 mole, 94%), m.p. 73-74.5°.

Anal. Calcd. for C₈H₁₀Cl₃NO: C, 37.16; H, 3.90; N, 5.41; C1, 41.14. Found: C, 37.25; H, 3.74; N, 5.39; C1, 41.17.

Hydrolysis of 5-Diethylamino-2,2 ,4-trichloro-3(2H) -furanone.--8 solution of **5-diethylamino-2,2,4-trichlorofuranone** (18.0 g., 0.064 mole) in methanol *(50* mi.) and 10% hydrochloric acid (50 ml.) was refluxed for 24 hr. The methanol was distilled and a yellow oil separated. The mixture was refluxed until the oil dissolved (1 hr.) and was allowed to cool. Carbon dioxide was evolved during the hydrolysis. The cooled solution was extracted with ether $(3 \times 100 \text{ ml.})$ and the ethereal solution was dried over anhydrous magnesium sulfate. Evaporation of the ether left a tan oily residue. A small portion of the oil was treated with excess aqueous sodium dichromate solution and yielded chloroacetic acid. The infrared spectrum was identical to that of an authentic sample. Thionyl chloride (15 g., 0.125 mole) was added to the major portion of the oil and the solution was warmed at 55" for 1 hr. The excess thionyl chloride was removed *in vacuo* and methanol (50 ml.) was added. The solution was refluxed for 0.5 hr. and the excess methanol was removed in *uacuo.* Distillation of the residue gave methyl chloropyruvate (3.1 g., 0.023 mole, 36%), b.p. 65-75 \degree (4-10 mm.); reported b.p. 78° (13 mm.)¹⁵; λ_{OH} (cm.⁻¹) 3450, $\lambda_{\text{C=0}}$ 1765, 1725 in the pure liquid.

The aqueous reaction mixture after extraction with ether was made alkaline with 20% sodium hydroxide solution and p-toluenesulfonyl chloride (20 g., 0.1 mole) was added. The mixture was shaken for 1 hr. and on chilling a solid separated. Recrystallization of the solid from methanol-water gave **N,N-diethyl-p-toluenesulfonamide** (4.3 g., 0.19 mole, $30\%,$ m.p. 60° ; reported m.p. $60^{\circ}.$ ¹⁶ The infrared spectrum was identical with that of an authentic sample.

Methyl Chloropyruvate.--A solution of methyl pyruvate $(51.0 \text{ g.}, 0.5 \text{ mole})$ in carbon tetrachloride (100 ml.) was stirred while sulfuryl chloride (67.0 g., 0.5 mole) was added dropwise over a period of 48 hr. The carbon tetrachloride and unchanged sulfuryl chloride were removed *in vacuo* and distillation produced methyl pyruvate (24 **g.),** b.p. 30-50' *(ca.* 15 mm.), fraction I1 (2 g.), b.p. 50-70" (4-15 mm.) and fraction III (30 g.), b.p. $70-75^{\circ}$ (4-5 mm.), n^{23} D 1.4460. Fraction I11 was redistilled giving methyl pyruvate (9.0 **g.,** total 33 g., 65%) and methyl chloropyruvate (21 g., 0.15 mole, 85% based on recovered starting material), b.p. 52° (1.1 mm.), $n^{27}D$ 1.4485, λ_{OH} (cm.⁻¹) 3450, $\lambda_{\text{C=0}}$ 1765, 1725 on the pure liquid. The infrared spectrum was identical to that of the sample prepared as described previously.

Anal. Calcd. for $C_4H_5ClO_3$: C, 35.18; H, 3.69; Cl, 25.97. Found: C, 34.47; H, 3.81; C1, 26.46.

Methyl **Chloropyruvate-2,4-dinitrophenylhydrazone.** A. **In** Methanol.-Methyl chloropyruvate (3.1 g., 0.023 mole) was disslolved in methanol and **2,4-dinitrophenylhydrazine** that of the samp

Anal. Calcd.

25.97. Found:

Methyl Chlorn

In Methanol.—

was dissolved in

(15) J. Ratusky a

 $(3.5 \text{ g.}, 0.0175 \text{ mole})$ was added. The mixture was warmed and shaken and a yellow solid separated. Recrystallization from methanol gave methyl methoxypyruvate 2,4-dinitrophenylhydrazone (0.74 g., 0.0024 mole, 14%), m.p. 197.5-198°, $\lambda_{C=0}$ (cm.⁻¹) 1710, $\lambda_{C=0-0}$ 1100 in CHCl₃, λ_{max} C_2H_5OH 218 μ (log ϵ 4.05), 250 (4.01).

Anal. Calcd. for $C_1H_{12}N_4O_7$: C, 42.31; H, 3.85; N, 17.95; C1, none. Found: C, 42.19; H, 3.71; N, 17.28, 18.27; C1, none.

Concentration of the mother liquor and chilling separated impure methyl **chloropyruvate-2,4-dinitrophenylhydrazone** (1.25 g., 0.0039 mole, 22%), m.p. 143-146°. The infrared spectrum was essentially identical with that of the sample prepared in the following manner.

B. In Hydrochloric Acid.---A mixture of 2,4-dinitrophenylhydrazine (3.96 g., 0.02 mole) and 12 *iV* hydrochloric acid (200 ml.) was added to a mixture of methyl chloropyruvate (2.72 g., 0.02 mole) and 12 *N* hydrochloric acid (50 ml.). The mixture was shaken for 1 hr. and a yellow solid separated. Cold water (150 ml.) was added and filtration produced a yellow solid. The solid was washed with water and dried in a vacuum desiccator for 24 hr. Recrystallization from benzene gave methyl chloropyruvate 2,4-dinitrophenylhydrazone (5.93 g., 0.019 mole, 95%), m.p. 156-158', **XC-o** (crn.-') 1700 in Nujol, **Xmax** C2H60H 217 (log *E* 4.05), 251 (4.00).

Anal. Calcd. for C₁₀H₉N₄O₆: C, 37.93; H, 2.86; N, 17.69; C1, 11.20. Found: C, 37.59; H, 2.81; N, 17.59; C1, 11.06.

5-Dimethylamino-2,2,4-trichloro-3(2H)-furanone (IVb).-A solution of N,N-dimethyl-2-chloroacetamide (12.1 g., 0.1 mole) in methylene chloride (50 ml.) was stirred at 0° and oxalyl chloride (25.4 g., 0.2 mole) was added dropwise. The solution was allowed to warm up to room temperature and was stirred for 24 hr. The methylene chloride was removed *in vacuo* and the residue was recrystallized from acetonewater. One further recrystallization from methylene chloride-hexane (with charcoal) gave 5-dimethylamino-2,2,4 trichloro-3(2H)-furanone (20.1 g., 0.087 mole, 87%), m.p. $114 - 116$ °.

Anal. Calcd. for C₆H₅Cl₃NO₂: C, 31.26; H, 2.62; N, 6.08; C1, 46.15. Found: C, 31.47; H, 2.62; N, 6.25; C1,45.98.

5-Methylanilino-2,2,4-trichloro-3(2H)-furanone (IVc).-**A** solution of N-methyl-2-chloroacetanilide (8.0 g., 0.044 mole) in methylene chloride (100 ml.) was stirred while oxalyl chloride (11.1 g., 0.088 mole) was added. The solution was refluxed at 35-40' for 3 hr. and then the methylene chloride was removed in *vacuo.* Recrystallization of the residue (with charcoal) from methylene chloride-hexane gave 5-methylanilino-2,2,4-trichloro-3(2H)-furanone (11.7) g., 0.040 mole, 91%), m.p. 149-150".

Anal. Calcd. for $C_{11}H_8C_{13}NO_2$: C, 45.16; H, 2.76; N, 4.79; C1, 36.36. Found: C, 45.43; H, 2.28; N, 5.00; C1, 36.36.

S-Diphenylamin0-2,2,4-trichloro-3(2H)-furanone (IVd) .- A solution of N,N-diphenyl-2-chloroacetamide (12.25 **g.,** 0.05 mole) and oxalyl chloride (13.0 g., 0.11 mole) in chloroform (70 ml.) was refluxed for 12 hr. The chloroform was removed *in vacua* and the residue was dissolved in acetone. The addition of water and chilling separated a yellow solid. One recrystallization from acetone-water and one (with charcoal) from methylene chloride-hexane gave 5-diphenyl**amino-2,2,4-trichloro-3(2H)-furanone m** a white solid (14.9 g., 0.042 mole, **84%),** m.p. 166-167'.

N, 3.95; C1, 30.00. Found: C, 53.96; H, 2.79; **N,** 3.77; Cl, 30.04. Anal. Calcd. for C₁₆H₁₀Cl₃NO₂: C, 54.19; H, 2.84;

S-Diethylamino-2,2-dichlor04-phenyl-3(2H)-furanone (IVe).-A solution of N,N-diethylphenylacetamide (19.1 g., 0.1 mole) in methylene chloride (100 ml.) was stirred while oxalyl chloride (25.4 *g.,* 0.2 mole) was added dropwise. The solution was stirred for 3 hr. and the methylene chloride was removed *in vacuo*. The residue was dissolved

⁽¹⁵⁾ J. **Ratusky and F. gorm,** *Chem. Eisly,* **51, 1091 (1957).**

⁽¹⁶⁾ R. S. Shriner, R. C. **Fuson, and** D. *Y.* **Curtin, "The Syetematic Identification of Organic Compounds,"** John **Wiley and Sons, Inc., New York.** N. *Y.,* **1956, p. 288.**

in acetone and treated with charcoal. Chilling and the addition of water separated a tan solid. Recrystallization from acetone-water gave **5-diethylamino-2,2-dichloro-4phenyl-** $3(2H)$ -furanone (17.2 g., 0.057 mole, 57%), m.p. 119-121°.

Anal. Calcd. for $C_{14}H_{16}Cl_2NO_2$: C, 56.01; H, 5.04; N, 4.67; C1, 23.62. Found: C, 55.95; H, 5.02; N, 4.76; C1, 23.65.

Hydrolysis of 5-Diethylamino-2,2-dichloro-4-phenyl-3- (2H)-furanone.-A mixture of **5-diethylamino-2,2-dichloro-**4-phenyl-3(2H)-furanone (8.0 g., 0.027 mole), 10% hydrochloric acid (100 ml.), and acetone (20 ml.) was refluxed for 24 hr. The resulting mixture was extracted with ether $(2 \times$ 100 ml.) and the ethereal extract was extracted with saturated sodium bicarbonate solution until carbon dioxide was no longer evolved. The bicarbonate solution was acidified with 12 *N* hydrochloric acid and extracted with ether $(2 \times$ 100 ml.). The ethereal solution was dried over anhydrous magnesium sulfate and treated with charcoal. Concentration of the solution to a small volume and the addition of hexane produced a white solid. Recrystallization from ether-hexane gave phenylpyruvic acid (2.7 g., 0.016 mole, 59%), m.p. $154-155^{\circ}$; reported m.p. $150-154^{\circ}$.¹⁷ The infrared spectrum was identical with that of an authentic sample.¹⁸

The aqueous portion of the reaction mixture after extraction with ether was basified with 20% sodium hydroxide solution and *p*-toluenesulfonyl chloride (5 g., 0.026 mole) was added. The mixture was shaken for 24 hr. and chilling separated a white solid. Recrystallization from methanolwater gave **N,N-diethyl-p-toluenesulfonamide** (4.8 g., 0.021 mole, 78%), m.p. 60° ; reported m.p. 60° .¹⁶ The infrared spectrum was identical with that of an authentic sample.

Reaction **of N,N-Diethyl-2-chloroacetamide** and Bromoacetyl Bromide.-- A solution of N,N-diethyl-2-chloroacetamide (14.9 g., 0.1 mole) and bromoacetyl bromide (20.1 g., 0.1 mole) in methylene chloride (100 ml.) was stirred for 72 hr . The resulting solution was chilled and water (100 ml.) was added. The methylene chloride solution was separated and dried over anhydrous magnesium sulfate. The methylene chloride waa evaporated *in vacuo* and distillation gave a liquid (17.8 g.), b.p. 75-85" (1.0-1.3 mm.). The liquid was washed with saturated sodium bicarbonate solution (50 ml.) and dried over anhydrous magnesium sulfate. Fractional distillation gave a forerun $(3.7 g.)$, b.p. $65-71°$ $(0.65 mm.)$ and N,N-diethyl-2-bromoacetamide (7.9 g., 0.041 mole, 41%), b.p. 74-75' (0.55 mm.), *72%* 1.4876; reported b.p. identical with that of an authentic sample. The infrared spectrum of the forerun indicated that it was composed primarily of N,N-diethyl-2-chloroacetamide.

(19) W. E. Weaver and W. M. Whaley, *J. Am. Chem. Soc.,* **69, 515 (1947).**

The Dimethyl-p-dioxanes and the 2,5-Dibutyl-p-dioxanes

E. K. SUMMERBELL, ANNA LOUISE BURLINGAME, DAVID R. DALTON, AND CECILE KAPLAN DALTON

Chemical Laboratories of Northwestern University, Evanslon, Illinois

Received July 9, 1968

The isomeric dimethyl-p-dioxanes have been synthesized. Contrary to former reports, their boiling points are consistent with current theory. The boiling points of the 2,5-di-n-butyl-p-dioxanes are anomalous.

Many of the properties of the disubstituted p-dioxanes parallel closely those of the disubstituted cyclohexanes. The preferential formation¹⁻⁴ under equilibration conditions of the trans-2,3-, trans-2,5 and $cis-2.6$ -disubstituted p -dioxanes, the potentially diequatorial forms of the assumed chair structures, 4 is of fundamental significance. Also, alkalicatalyzed equilibration of the dicarboxylic acid esters resulted in conversions to the theoretically more stable forms.^{1,2,4} In contrast, the reported values for the normal boiling points of dimethylp-dioxanes seem peculiar, since they cover an unexpectedly large span, 114-135°, twice that for the corresponding dimethylcyclohexanes, 119.4-129.5°.6 To investigate this seeming anomaly, we have prepared the four missing members of the series of seven possible isomers.

The structure and properties of trans-2,5-dimethyl-p-dioxane (I) are known with certainty, since it was prepared⁶ by the lithium aluminum hydride reduction of **trans-2,5-bis(iodomethyl)-p**dioxane,² a method that should not cause isomerization.' The recently reported⁸ 2,2-dimethyl- p dioxane (VII) seems also to have been made under conditions that should give a reasonably pure substance. The material reported as 2,6-dimethyl-pdioxane is presumably the *cis* isomer.⁹ as it probably was prepared by reducing a mercury-containing intermediate that was also converted by iodine treatment to a compound later proved¹ to be **cis-2,6-bis(iodomethyl)-p-dioxane.** Other reports of the preparation of dimethyl-p-dioxanes in the literature could give at best mixtures of isomers,

- **(6) E. Augdahl,** *Acto Chem. Scand.,* **9, 1237 (1955).**
- **(7) D.** *8.* **Noyoe and D. B. Denney,** *J. Am. Chem. Soc.,* **73, 5743 (1950).**
- *(8)* **R. I. Meltser, A. D. Lewis, and A. Fischmann,** *J.* **Org.** *Chem.,* **24, 1763 (1959).**

⁽¹⁷⁾ R. M. Herbst and D. **Shemin, "Organic Syntheses," Coll.** Vol. **11, John Wiley and Sons, Inc., New York, N. Y., 1959, p. 519.**

⁽¹⁸⁾ K and K Laboratories, Inc., Jamaica, New York.

⁽¹⁾ R. K. Summerbell and J. R. Stephens, *J. Am. Chem.* Soc., **76, 731 (1954).**

⁽²⁾ R. K. Summerbell and J. R. Stephens, *ibid.,* **76, 6401 (1954).**

⁽³⁾ R. K. Summerbell, *G.* **Lestina, and H. Waite,** *ibid.,* **79, 234 (1957).**

⁽⁴⁾ R. K. Bummerbell and G. Lestina, *ibid.,* **79, 3878 (1957).**

⁽⁵⁾ G. A. Haggis and L. N. **Owen,** *J. Chem. Soc.,* **408 (1953).**

⁽⁹⁾ A. *N.* **Nesmeyanov and I. F. Lutsenko,** *Bull. mad. sei. USSR Classe. sei. chim.,* **296 (1943).**