[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Monoalkyldioxanes

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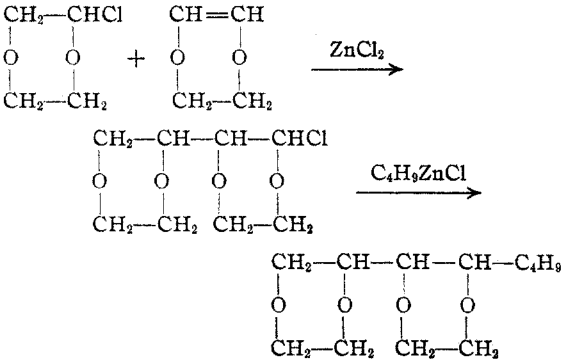
Methods of synthesizing dialkyl-, diaryl-, and monoaryldioxanes have been reported previously.[1,2] The analogous method is applied here to the problem of the monoalkyldioxanes. Variations in the procedure indicate the best yields to be obtained by adding pure monochlorodioxane to the Grignard solution.

In the previous work on dialkyldioxanes,[2] it was found advantageous to treat the Grignard reagent with zinc or cadmium chlorides before carrying out the reaction with the 2,3-dichlorodioxane. As there is little possibility of a dehalogenating side reaction, no advantage was anticipated in the present case, and none was found.

Because of the tendency of monochlorodioxane to decompose on standing, it was always freshly prepared before each reaction. Monochlorodioxane is best made by adding dry hydrogen chloride to dioxene at 0° and distilling the resulting mixture. The yields of monochlorodioxane are lowered by using benzene or ethyl ether as solvents. The conversion of dioxene to monochlorodioxane seems to be incomplete, even with the use of excess hydrogen chloride, since slight amounts of dioxene are recovered on distillation of the reaction product.

A mixture of dioxene and monochlorodioxane, in the presence of polymerizing catalysts, when treated with a Grignard reagent yields, besides the expected alkyldioxane, a small amount of a solid product. No solid by-product was obtained in cases where the monochlorodioxane was distilled before the reaction with the Grignard reagent or when the polymerizing catalysts were omitted. The compound obtained by the use of the butyl Grignard reagent in the presence of zinc chloride had the empirical formula $C_{12}H_{22}O_4$. As the compound is without any very reactive functional groups, the four oxygen atoms are probably constituents in two dioxane rings. From these data formula I, 2-butyl-3-dioxanyldioxane, can be advanced as the possible structure of the compound. As acyl halides[3] and α-chloroethers[4,5] in the presence of catalysts may be added to ethylenic hydrocarbons, the probable mechanism by which the 2-butyl-3-dioxanyldioxane is formed is shown by the equation.



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Additional evidence for the structure of the solid has been secured by similarly preparing the corresponding by-product 2-ethyl-3-dioxanyldioxane with the use of the ethyl Grignard reagent.

A New Synthesis of Substituted Dioxanes.—Another synthesis of substituted dioxanes was suggested by the fact that β-chloroethyl ether is converted to dioxane when heated with 5% sodium hydroxide at 200°,[6] or by other reagents.[7]

This method has been applied in synthesizing ethyldioxane from β-chloroethyl β-bromo-α-ethylethyl ether. A mixture of equivalent amounts of acetaldehyde and ethylene chlorohydrin was treated with dry hydrogen chloride at 0° to form β-chloroethyl α-chloroethyl ether.[8] This ether when brominated according to the method of Boord[9] yielded β-chloroethyl α,β-dibromoethyl ether. The reaction of this substance with ethylmagnesium bromide resulted in the desired β-chloroethyl β-bromo-α-ethylethyl ether. When this ether was treated with 10% potassium hydroxide at 200° for three and one-half hours, a 17% yield of ethyldioxane was obtained. By varying the starting materials and Grignard reagents used, this appears to be a general method for the synthesis of many other substituted dioxanes.

Properties of the Monoalkyldioxanes.—The homologous series of the monoalkyldioxanes

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[1] Summerbell and Christ, THIS JOURNAL, **55**, 4547 (1933).

[2] Summerbell and Bauer, *ibid.*, **57**, 2364 (1935); **58**, 759 (1936).

[3] Norris and Couch, *ibid.*, **42**, 2329 (1920).

[4] Straus and Thiel, *Ann.*, **525**, 151 (1936).

[5] Nenitzescu and Przemetzki, *Ber.*, **69**, 2706 (1936).

[6] French Patent 711,595; *C. A.*, **26**, 1947 (1932).

[7] British Patent 435,110; *C. A.*, **30**, 1387 (1936).

[8] Grignard and Purdy, *Bull. soc. chim.*, **31**, 982 (1921); *Compt rend.*, **175**, 200 (1922).

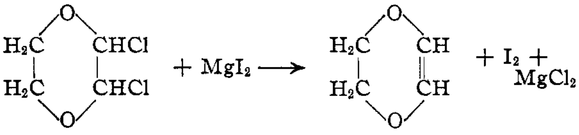
[9] Boord, THIS JOURNAL, **52**, 653 (1930).

exhibits a uniform variation in physical properties. However, the relationship of refractive index and density appears to be uncommon,[10] in that the slope of the plot of refractive indices of the monoalkyldioxanes, against density, is negative. Methyldioxane, as is dioxane itself, is infinitely soluble in water. Ethyldioxane dissolves to a considerable extent and propyl and butyldioxanes are not appreciably soluble. The lower members of the series have a characteristic, slightly displeasing, ethereal odor. The unpleasantness of the odor increases with higher members of the series.

Dioxane forms addition products with picric acid[11] and hydroquinone[12] which can serve as derivatives. The action of these reagents was tried on the monoalkyldioxanes, but in no case was it possible to isolate an addition compound.

A New Preparation of Dioxene.—Previously dioxene has been prepared only by the action of aliphatic Grignard reagents on 2,3-dichlorodioxane.[2] The reaction of light metals with 2,3-dichlorodioxane was found by Böeseken[13] to result only in tar. He also noted in the reaction of 2,3-dichlorodioxane with sodium iodide in boiling acetone that free iodine was liberated and a precipitate of sodium chloride formed, but he was not able to isolate dioxene.

As the reaction of inorganic iodides on α,β-dihalogen compounds is a method of obtaining double bonds under mild conditions,[14] it seemed desirable to apply this procedure to the synthesis of dioxene. It has been found that a mixture of magnesium and magnesium iodide in dry ether dehalogenates 2,3-dichlorodioxane to yield dioxene. This combination is useful because magnesium iodide is appreciably soluble in ether.



$$Mg + I_2 \longrightarrow MgI_2$$

Furthermore magnesium reacts with the liberated iodine to reform magnesium iodide. The formation of dioxene probably occurs through the intermediate formation of 2,3-diiododioxane.[15]

The use of the combination of magnesium and magnesium iodide in anhydrous solvents as a dehalogenating agent for α,β-dihalogen compounds holds many possibilities of being applicable to those compounds which may be decomposed under more vigorous conditions.

Experimental

Monoalkyldioxanes.—The properties and analyses of the monoalkyldioxanes are given in the tables.

TABLE I

PROPERTIES OF MONOALKYLDIOXANES

Alkyl group	B. p., °C.	Mm.	d^{20}_4	n^{20}_D	MR_D[b] Calcd.	Found
Methyl-	109–110	746.5	0.977	1.4188	26.38	26.39
Ethyl-	132.5–133	750	.955	1.4263	30.99	31.17
n-Propyl-	155.6–157.1	746[a]	.943	1.4298	35.61	35.64
n-Butyl-	178–179	735[a]	.932	1.4336	40.23	40.26
Allyl-	156–158	747.6[a]	.937	1.4442	35.14	36.35

[a] Corrected temperatures. [b] The calculated values were obtained by using the atomic values from Gilman, "Organic Chemistry," p. 1738. The found values are calculated from the formula of Lorenz and Lorentz.

TABLE II

ANALYSES OF MONOALKYLDIOXANES

Alkyl group	Formula	Percentage composition Calcd. C	H	Found C	H
Methyl-	$C_5H_{10}O_2$	58.82	9.80	58.53	9.77
Ethyl-	$C_6H_{12}O_2$	62.07	10.34	62.31	10.24
n-Propyl-	$C_7H_{14}O_2$	64.57	10.76	64.31	10.74
n-Butyl-	$C_8H_{16}O_2$	66.62	11.62	66.22	11.19
Allyl-	$C_7H_{12}O_2$	65.57	9.37	65.39	9.58

Allyldioxane.—The procedure that has given the most satisfactory yields of the monoalkyldioxanes was that used in synthesizing allyldioxane. This method will be given in detail.

The allyl Grignard reagent was prepared from 181.5 g. (1.5 moles) of allyl bromide, 36.4 g. (1.5 moles) of magnesium and 600 cc. of dry ether.[16]

The monochlorodioxane was prepared by conducting, with stirring, 2.4 moles of dry hydrogen chloride into 51.6 g. (0.6 mole) of dioxene at 0°. The resulting mixture, on fractional distillation, yielded 50 g. (68.5%) of monochlorodioxane, b. p. 57–65° (25 mm.).

The monochlorodioxane was then added dropwise to the allylmagnesium bromide solution. The reaction mixture was stirred for one-half hour after all the monochlorodioxane had been added. Then excess Grignard reagent was hydrolyzed by slowly adding iced, dilute hydrochloric acid and the ether layer was separated, dried over sodium sulfate, decanted and then fractionally distilled. The fraction which distilled at 148–157° was collected as allyldioxane; yield, 37.8 g. (72.5%). The material was refluxed over sodium for several hours and fractionally distilled twice, b. p. 156–158° (corr.) at 747.6 mm.; d^{20}_4 0.937; n^{20}_D 1.4442.

The monoalkyldioxanes were purified by distillation from metallic sodium through a 40-cm. Podbielniak type column. In most cases the refractive indices of the first

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(10) Kurtz and Ward, *J. Franklin Inst.*, **222**, 563 (1936).

(11) A. Faworsky, *J. Russ. Phys.-Chem. Soc.*, **38**, 741 (1906).

(12) Evans and Dehn, THIS JOURNAL, **52**, 3204 (1930).

(13) Böeseken, Tellegen and Henriquez, *ibid.*, **55**, 1284 (1933).

(14) Finkelstein, *Ber.*, **43**, 1528 (1910).

(15) C. F. Van Duin, *Rec. trav. chim.*, **43**, 341 (1924).

(16) Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

and last portions of the distillate were the same. The allyldioxane, in contrast to the other alkyldioxanes, decomposed considerably when refluxed with sodium. The solid decomposition products were shaken with dilute sodium hydroxide and benzoyl chloride, extracted with ether, and, after drying over sodium sulfate, the ether was allowed to evaporate. A small amount of crystals formed on the side of the beaker and a viscous oil remained on the bottom. The crystals were collected and recrystallized three times from dilute alcohol, m. p. 70°. A mixed melting point with authentic ethylene dibenzoate was at 70–71°. This indicates ethylene glycol to be a reaction product of allyldioxane and sodium.

Reaction of Monochlorodioxane with Butyl Grignard Reagent Using Zinc Chloride.—The Grignard reagent was prepared from 205 g. (1.5 moles) of butyl bromide, 36.4 g. (1.5 moles) of magnesium and 700 cc. of dry ether. To this Grignard reagent was added 204 g. (1.5 moles) of anhydrous zinc chloride dissolved in 300 cc. of dry ether. The mixture was then refluxed for one hour on a water-bath kept at 40°.

The monochlorodioxane was prepared by dissolving 51.6 g. (0.6 mole) of dioxene in 100 cc. of dry benzene and passing into the solution at 0° 1.5 moles of dry hydrogen chloride. The solution was allowed to stand for three hours at room temperature, the color changing from colorless to yellow. Then excess hydrogen chloride was removed under the reduced pressure of the water pump.

The solution of monochlorodioxane was added dropwise to the organometallic mixture at 0°. The reaction mixture was allowed to stand at room temperature for ten hours, and was then refluxed on a water-bath for six hours. The flask was cooled in an ice-bath, and cold water slowly added to the reaction mixture. The precipitate that formed was dissolved by adding dilute sulfuric acid and the ether layer was then separated, dried over sodium sulfate, decanted and fractionally distilled. A fraction which distilled at 40–65° at 18 mm. was collected. The liquid residue which remained solidified on cooling. The fraction of butyldioxane was distilled twice from sodium: yield, 9.5 g. (11%); b. p. 178.2–179.2° (corr.) at 735 mm.; d^{20}_{4} 0.932; n^{20}_{D} 1.4336.

2-Butyl-3-dioxanyldioxane.—The solid residue from the first distillation of butyldioxane was extracted with petroleum ether, treated with norite and the solvent evaporated. The crystalline residue (1 g.) was recrystallized from dilute alcohol, needles, m. p. 101–102°. The solid was insoluble in water and was not affected by dilute hydrochloric acid or dilute sodium hydroxide. It dissolved in concentrated sulfuric acid without darkening. The material was recovered unchanged after being dissolved in acetyl chloride for one-half hour. The molecular weight, determined by the cryoscopic method using benzene, was found to be 242.

Anal. Calcd. for 2-butyl-3-dioxanyldioxane ($C_{12}H_{22}O_4$): C, 62.61; H, 9.56; mol. wt., 230. Found: C, 62.38, 62.29; H, 9.47, 9.39.

A number of experiments were tried in attempts to increase the yield of the solid compound. Aluminum chloride and zinc chloride were used as catalysts with mixtures of monochlorodioxane and dioxene before the reaction with butylmagnesium bromide. Benzene and carbon disulfide were employed as solvents in the preparation of monochlorodioxane. In most cases a small amount of the solid was obtained. However, the polymerizing agents tended to lead to the formation of tars. A later experiment using magnesium bromide as the catalyst in the synthesis of 2-ethyl-3-dioxanyldioxane appeared to be more satisfactory.

2-Ethyl-5-dioxanyldioxane.—Approximately 0.28 mole of dry hydrogen chloride was bubbled into a solution of 12 g. (0.14 mole) of dioxene and 200 cc. of dry benzene. The resulting mixture was allowed to stand at room temperature for four and one-half hours after adding 7.4 g. of dioxene and a solution of magnesium bromide prepared from one-half gram of bromine in 5 cc. of ether and excess magnesium. Excess hydrogen chloride was then removed from the colorless, turbid solution under the reduced pressure of the water pump.

To this solution was added a filtered Grignard reagent prepared from 64.8 g. of ethyl bromide, 14.4 g. of magnesium and 300 cc. of ether. After standing overnight, excess Grignard reagent was hydrolyzed by slowly adding dilute hydrochloric acid. The ether layer was separated, dried over sodium sulfate and fractionally distilled. A 3.6-g. fraction of ethyldioxane which distilled at 100–138° was collected. The residue (9.5 g.) did not crystallize on standing for several days in the refrigerator. It formed a glass on cooling with dry ice. The material was then heated in a bath at 150° under 20 mm. pressure. About 1 g. of distillate (ethyldioxane) was obtained. The residue contained a few crystals after standing for several days in the refrigerator. The mixture was dissolved in petroleum ether and decanted from some insoluble, colored tar. The petroleum ether was then evaporated and the residue warmed under reduced pressure to remove all the petroleum ether. The material did not crystallize on standing two weeks in the refrigerator. It was then vacuum distilled (1 mm.). The distillate formed an oily mass of crystals after several days. The crystals were filtered, and crystallized twice from dilute methanol: yield 0.5 g., m. p. 97.5°.

A mixed melting point with the solid from the butyldioxane synthesis (m. p. 102°) showed a large depression. The material is slightly soluble in water and easily soluble in organic solvents.

Anal. Calcd. for 2-ethyl-3-dioxanyldioxane ($C_{10}H_{18}O_4$): C, 59.40; H, 8.97. Found: C, 59.41; H, 9.02.

Ethyldioxane from β-Chloroethyl β-Bromo-α-ethylethyl Ether

α-Chloroethyl β-Chloroethyl Ether.—This ether was prepared according to the procedure of Grignard and Purdy[8] by conducting approximately 4 moles of dry hydrogen chloride into a mixture of 88 g. (0.67 mole) of paraldehyde and 161 g. (2 moles) of ethylene chlorohydrin at 0°. The yield of crude, dry α-chloroethyl β-chloroethyl ether was 227 g. (79%).

β-Chloroethyl α,β-Dibromoethyl Ether.—The crude α-chloroethyl β-chloroethyl ether (227 g. or 1.58 moles) was cooled to 0° in an ice-bath and 254 g. (1.58 moles) of bromine added in small portions over a period of two and one-half hours. The reaction product was then placed under reduced pressure to remove hydrogen chloride.

The material, yellow in color, separated into two layers on standing. The small top layer appeared to be water; yield, 420 g. (99%).

One-half, 210 g., of the β-chloroethyl α,β-dibromoethyl ether on distillation yielded a 154 g. (73%) fraction which distilled at 110–113° (12 mm.). This material was without color but turned light yellow on standing a short time. It fumed in air. A portion of the material was redistilled, b. p. 108° (12 mm.).

Anal. Calcd. for $C_4H_7OClBr_2$: total halogen, 73.33. Found: total halogen, 73.55.

β-Chloroethyl β-Bromo-α-ethylethyl Ether.—The unpurified β-chloroethyl α,β-dibromoethyl ether (210 g., 0.79 mole) was added during one hour to a solution at 0° of ethylmagnesium bromide prepared from 108.9 g. (1 mole) of ethyl bromide, 24 g. of magnesium and 450 cc. ether. The reaction mixture was stirred for one-half hour at room temperature. Then excess Grignard reagent was destroyed by slow addition of dilute hydrochloric acid and the ether layer was removed and dried over calcium chloride. After standing for two days the solution had a deep green color. The ether was then removed on a water-bath and the liquid residue vacuum distilled. A 42.5 g. (25%) fraction was obtained which distilled at 92° (12 mm.). The distillate was at first colorless but soon turned pink in color. After standing for two days it became dark amber in color.

A portion of the material was redistilled. A fraction which distilled at 92–93° (12 mm.) was colorless and remained so on standing; $d^{20}{}_4$ 1.388; $n^{20}{}_D$ 1.4770.

Anal. Calcd. for $C_6H_{12}OClBr$: total halogen, 53.55. Found: total halogen, 54.10.

Ethyldioxane.—Thirty grams of β-chloroethyl β-bromo-α-ethylethyl ether was refluxed for twenty-six hours with 30 g. of potassium hydroxide and 270 cc. of water. At the end of that time a test for halogen was obtained from the aqueous portion; however, a considerable amount of insoluble material remained. The mixture was divided into two equal portions. One portion was heated at 200–205° (bath temp.) in a monel metal bomb for one and one-half hours. The dark turbid solution was then extracted four times with a total of 150 cc. of ether. The combined ether extracts were dried over sodium sulfate and fractionally distilled. Eight-tenths gram (10%) of ethyl dioxane was obtained, b. p. 132–136°.

The other portion of the dihalogen ether and potassium hydroxide mixture was heated at 200–205° (bath temp.) for three and one-half hours. After working up the product as before, 1.4 g. (17%) of ethyldioxane was obtained, b. p. 132–136°.

Dioxene.—The reaction was carried out in a three-necked, five-liter flask equipped with a dropping funnel, bulbed condenser fitted with a calcium chloride tube and a mercury-sealed Hershberg stirrer.[17] In the flask were placed 82.6 g. (3.4 moles) of magnesium turnings and 1200 cc. of dry ether. Then 91.5 g. (0.4 mole) of iodine was added in small portions. The formation of the magnesium iodide occurred readily with the liberation of considerable amounts of heat. When the mixture became colorless, 314 g. (2 moles) of 2,3-dichlorodioxane mixed with 200 cc. of ether was added dropwise, with vigorous stirring, at such a rate that the color of the mixture due to the liberated iodine was never darker than light brown (nine hours). One-half hour after the addition of the last of the 2,3-dichlorodioxane, the mixture became colorless. It was then poured onto cracked ice and the ether layer separated, dried over sodium sulfate, decanted and fractionally distilled. A fraction which distilled at 93–95° was collected as dioxene: yield 84.3 g. (49%).

The synthesis of dioxene by this method has been carried out using varying proportions of magnesium iodide and 2,3-dichlorodioxane. Greater yields of dioxene were obtained with the use of larger amounts of magnesium iodide, and the reaction, particularly after a considerable amount of the 2,3-dichlorodioxane had been added, appeared to proceed more smoothly. In all cases the reaction proceeded at a decreasing rate. This is possibly due to coprecipitation of the iodide ion with the insoluble magnesium chloride. The effect of varying the ratio of magnesium iodide to 2,3-dichlorodioxane on the yield of dioxene is shown in the following table.

Ratio, moles iodine/ moles 2,3-dichlorodioxane	Yield, %
1:20	31
1:10	44
1:5	49

Summary

A series of monoalkyldioxanes has been prepared for the first time. The densities, refractive indices and boiling points vary in a uniform manner with increasing size of alkyl group. An uncommon relationship of refractive index and density exists for the series.

A solid by-product from the synthesis of the monoalkyldioxanes has been indicated to be the 2-alkyl-3-dioxanyldioxane. The mechanism for the formation and a method for the synthesis of the compounds are given.

A general method for the synthesis of substituted dioxanes by means of substituted β-halogenethyl ethers has been discussed. The procedure has been applied in the synthesis of ethyldioxane from β-chloroethyl β-bromo-α-ethylethyl ether.

A mixture of magnesium and magnesium iodide in dry ether has been found to be a new and excellent reagent for dehalogenating α,β-dihalogen compounds. It was used in the synthesis of dioxene from 2,3-dichlorodioxane.

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[17] Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).