

formed by oxidative coupling of two molecules of the Ivanov reagent.⁵ McKenzie and Ritchie⁶ prepared the succinic acid corresponding to II by treatment of α -chloro- α -phenylpropionic acid with either metallic copper or ethylmagnesium bromide. They assigned the racemic configuration to this acid, which split off water at the melting point to give the anhydride II, m.p. 159–160°. In the present work, the low yields of characterized products do not preclude the possibility that some of the meso-form of *sym.* dimethyldiphenylsuccinic acid, which does not form the corresponding anhydride at its melting point,⁶ was formed also. However, it is felt that if an appreciable amount had been present, it would have interfered considerably with the purification of the minute amount of α -methyltropic acid formed in the reaction. If one can assume that the racemic form of the succinic acid is indeed formed to the near exclusion of the meso-form, a transition state involving minimum phenylphenyl interaction similar to the one proposed by Zimmerman and Traxler² for the Ivanov reaction of phenylacetic acid with benzaldehyde may also be involved in the oxidative coupling reaction. However, any extension of these stereochemical mechanisms to the coupling reactions of the α -chloro derivatives studied by McKenzie and Ritchie⁶ must account for their observation that the use of metallic silver led to the meso-form of *sym.* dimethyldiphenylsuccinic acid in contrast to the production of the racemic form when metallic copper was used.

It should be noted that the purpose of this work was to prepare α -methyltropic acid by a reasonably unequivocal method. Foster and Ing⁷ reported the preparation of this acid by the action of nitrous acid on ethyl β -amino- α -methyl- α -phenylpropionate followed by hydrolysis of the hydroxy ester, but later found⁸ that their hydroxy acid was actually the isomeric rearranged product, α -benzyl-lactic acid, m.p. 98°. The α -methyltropic acid obtained in the present work melted at 86–87°.

EXPERIMENTAL

To a stirred solution of isopropylmagnesium bromide in ether (prepared from 87 g. of isopropyl bromide and 16 g. of magnesium) was added, with cooling, a solution of α -phenylpropionic acid (35 g., 0.23 mole) in 500 ml. of dry toluene. The mixture was then stirred and refluxed overnight. After removal of the ether by distillation, gaseous formaldehyde (generated from 23 g. of trioxane) was introduced into the stirred refluxing mixture over a 4-hr. period by means of a stream of dry nitrogen. The mixture was then stirred overnight at room temperature, cooled in an ice bath and treated with excess aqueous ammonium chloride

(5) D. Ivanov and A. Spassov, *Bull. soc. chim. France* [5] 2, 76 (1935), reported the formation of *sym.* diphenylsuccinic acid by oxidation of the Ivanov reagent of phenylacetic acid with either oxygen (8% yield) or bromine (22% yield).

(6) A. McKenzie and A. Ritchie, *Ber.*, 71, 643 (1938).

(7) R. Foster and H. R. Ing, *J. Chem. Soc.*, 938 (1956).

(8) R. Foster and H. R. Ing, *J. Chem. Soc.*, 925 (1957).

followed by dilute sulfuric acid. The layers were separated and the toluene layer was extracted with excess 10% sodium carbonate solution. Acidification of the carbonate extract gave an oil which was taken up in ether and dried over anhydrous magnesium sulfate. Filtration and removal of the ether by distillation followed by vacuum (0.5 mm.) distillation of the residue gave three fractions, b.p. 90–135° (7.9 g., n_D^{25} 1.5268), b.p. 135–150° (4.5 g., n_D^{25} 1.5510), and b.p. 150–215° (5.8 g., n_D^{25} 1.5569). The first fraction was largely unreacted α -phenylpropionic acid. The other two fractions were treated separately with saturated sodium bicarbonate solution. Insoluble neutral material (a larger amount from the third fraction) crystallized from the second and third fractions and was filtered. Recrystallization from a benzene-cyclohexane mixture gave colorless *sym.* dimethyldiphenylsuccinic anhydride, m.p. 157–159° (lit.,⁶ m.p. 159–160°).

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75; O, 17.12. Found: C, 77.08; H, 5.98; O, 16.97.

The infrared spectrum of this product indicated the presence of a phenyl, a C-methyl, a five-membered anhydride ring, and the absence of hydroxyl.

The filtered bicarbonate extract of the middle fraction was acidified with dilute hydrochloric acid. The precipitated oil was taken up in ether and dried over anhydrous magnesium sulfate. Filtration, removal of the ether by distillation and trituration of the residue with pentane gave a small amount of a solid acid. Recrystallization from an ethylene dichloride-pentane mixture gave α -methyltropic acid, m.p. 86–87°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; O, 26.65. Found: C, 66.37; H, 6.89; O, 26.82.

The infrared spectrum was entirely consistent with the assigned structure.

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Monochloro-*p*-dioxane and Trichloro-*p*-dioxanes

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Among the characterized chlorination products of *p*-dioxane, the dichloro and tetrachloro derivatives predominate.¹ In the chlorination of *p*-dioxane at 90°, the second chlorine atom is introduced more readily than the first as indicated by the failures to isolate a monosubstituted product.² However, it appears that the ease of introduction decreases for the third chlorine atom as evidenced by the very high yields of 2,3-dichloro-*p*-dioxane.

(1) R. C. Elderfield, *Heterocyclic Compounds*, John Wiley and Sons, Inc., New York, 1957, Volume 6, p. 11.

(2) Ref. (1), p. 10.

Continued chlorination over extended periods of time or under more severe conditions gives rise to tetrachloro-*p*-dioxanes.³

In the chlorination at low temperature in carbon tetrachloride solution the reaction proceeds slowly enough to permit the isolation of intermediate products. If the chlorination of *p*-dioxane is interrupted at a proper time, substantial quantities of monochloro-*p*-dioxane can be isolated by distillation,⁴ but the instability of the compound makes a quantitative determination in this way impossible. We have therefore treated the chlorination mixture with an excess of phenylmagnesium bromide. From the amount of monophenyl-*p*-dioxane⁵ isolated it was calculated that monochloro-*p*-dioxane had been formed to an extent of at least 34% at the time the chlorination was stopped. We have also determined by infrared spectroscopy that the dichloro-*p*-dioxane fraction in the low temperature chlorination consists of 2,5-dichloro-*p*-dioxane and both *cis*- and *trans*-2,3-dichloro-*p*-dioxane.

The introduction of chlorine at low temperatures into the two different 2,3-dichloro-*p*-dioxanes leads to the formation of two of the four possible 2,3,5-trichloro-*p*-dioxanes. Chlorination of *trans*-2,3-dichloro-*p*-dioxane in carbon tetrachloride solution at -5° produces a trichloro-*p*-dioxane, m.p. 41° , whereas chlorination of *cis*-2,3-dichloro-*p*-dioxane⁶ under similar conditions yields a trichloro-*p*-dioxane, m.p. 70° . A third trichloro-*p*-dioxane with the chlorine atoms in positions 2,2,3 was prepared by addition of chlorine to 2-chloro-*p*-dioxene.

EXPERIMENTAL

Monochloro-p-dioxane in the low temperature chlorination of p-dioxane. A solution of 100 ml. (1.14 moles) of *p*-dioxane in 100 ml. of carbon tetrachloride was cooled to -10° and chlorinated until crystals first appeared, about eight hours. After most of the solvent had been evaporated under reduced pressure, the major part of the reaction product ($\frac{2}{3}$) was subjected to a fractional distillation. There was obtained a fraction of 13.6 g., b.p. $30-50^{\circ}/35$ mm., consisting of mainly monochloro-*p*-dioxane and some dioxane. The remaining part of the reaction product ($\frac{1}{3}$) was added to a Grignard solution prepared from 24.3 g. (1 mole) of magnesium and 157 g. (1 mole) of bromobenzene. The mixture was poured on 1 kg. of ice and 50 ml. of sulfuric acid, and the ether layer was shaken with sodium bicarbonate solution and dried with calcium chloride. After evaporation of ether, the residue was distilled *in vacuo*, yielding 33 g. of a colorless product b.p. $76-85^{\circ}/1-1.5$ mm. This product was identified by means

(3) C. L. Butler and L. H. Cretcher, *J. Am. Chem. Soc.*, **54**, 2987 (1932).

(4) Monochloro-*p*-dioxane was isolated from the low temperature chlorination of *p*-dioxane for the first time by W. M. Smedley and G. H. Kalb in this laboratory. Determination of the yield was not attempted.

(5) R. K. Summerbell and L. N. Bauer, *J. Am. Chem. Soc.*, **57**, 2364 (1935).

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

of its infrared spectrum as a mixture of monophenyl-*p*-dioxane and diphenyl. Infrared analysis on the basis of the absorption peaks at 11.2 microns (monophenyl-*p*-dioxane) and 6.7 microns (diphenyl) showed that the mixture contained 63% monophenyl-*p*-dioxane. Based on starting material, *p*-dioxane, this would mean a 34% yield of monochloro-*p*-dioxane at the point of interruption of the chlorination. The Grignard reaction is assumed to proceed with 100% yield, and the 34% yield must therefore be considered as a minimum figure.

In another experiment the chlorination was continued to give mainly dichloro-*p*-dioxanes. An investigation of the infrared spectrum of the crude reaction product showed that it contained considerable amounts of *cis*-2,3-dichloro-*p*-dioxane.

Preparation of 2,3,5-trichloro-p-dioxane, m.p. 41°. A solution of 100 g. of *trans*-2,3-dichloro-*p*-dioxane in 100 ml. of carbon tetrachloride was chlorinated for 6.5 hr. under irradiation with ultraviolet light, while the temperature was kept between -5° and 0° . The mixture was fractionally distilled *in vacuo*, and the fractions with refractive indices higher than 1.50 were placed in the cold room. After several days, the highest boiling fraction ($60-62^{\circ}/0.5$ mm., n_D^{20} 1.5173) had separated 11.4 g. (9.3%) of crystals, which were filtered and dried on clay. M.p. 41° after recrystallization from pentane.

Anal. Calcd. for $C_4H_5O_2Cl_3$: C, 25.09%; H, 2.62%. Found: C, 25.16%; H, 2.51%.

In another run, the distillation gave fractions with higher refractive indices. On standing in the cold room, a mixture of trichloro-*p*-dioxane, m.p. 41° , and *sym.* tetrachloro-*p*-dioxane, m.p. 101° , crystallized. They can be separated by fractional crystallization from carbon tetrachloride.

When the new trichloro-*p*-dioxane was hydrolyzed by refluxing it with distilled water, and *p*-nitrophenylhydrazine hydrochloride was added, there was obtained 1.88 equivalents of the *p*-nitrophenylosazone of glyoxal. This proves the chlorine atoms to be in positions 2,3,5, giving rise on hydrolysis to one mole of glyoxal and 1 mole of glycolaldehyde.

Preparation of 2,3,5-trichloro-p-dioxane, m.p. 70°. A solution of 12 g. (0.077 mole) of *cis*-2,3-dichloro-*p*-dioxane⁶ in 75 ml. of carbon tetrachloride was chlorinated for 1 hr. at -10° . Strong irradiation with ultraviolet light had to be used to initiate the reaction. The liquid chlorination product did not solidify on cooling, but upon addition of 20 ml. of pentane and cooling to -20° there was obtained 1 g. (6.9%) of a colorless substance, m.p. $69-70^{\circ}$, after recrystallization from pentane.

Anal. Calcd. for $C_4H_5O_2Cl_3$: C, 25.09%; H, 2.62%. Found: C, 25.13%; H, 2.56%.

Assuming that the two chlorine atoms in the starting material have not changed their positions during the reaction, the compound must be assigned the structure of a 2,3,5-trichloro-*p*-dioxane since the only other possible structure, 2,2,3-trichloro-*p*-dioxane, is associated with a different compound.

Preparation of 2,2,3-trichloro-p-dioxane. To a solution of 40 g. (0.33 mole) of 2-chloro-*p*-dioxene⁶ in 50 ml. of carbon tetrachloride was added chlorine at -10° . The yellow color of the solution indicated the completion of the reaction. Distillation *in vacuo* yielded 48 g. (76%) of material, b.p. $60-61^{\circ}/1$ mm. A fraction of it was recrystallized several times from pentane at -50° and melted at $20-21^{\circ}$.

Anal. Calcd. for $C_4H_5O_2Cl_3$: C, 25.09%; H, 2.62%. Found: C, 25.20%; H, 2.61%.

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