Anal. Calcd. for $C_{10}H_6Cl_3NO_4$ (310.6): C, 38.85; H, 2.05; Cl, 34.40; N, 4.55. Found: C, 38.90; H, 2.29; Cl, 34.73; N, 4.55.

The product reacts exothermically with methanol to give methyl 3,4-dichlorooxanilate, identical with the product prepared from the cyclic anhydride II.

Methyl N-(Carboethoxy)-3,4-dichlorooxanilate (Vb).—A solution of N-carboethoxy-3,4-dichlorooxanilyl chloride (6.3 g., 0.02 mole) in a large excess of methanol (60 ml.) was allowed to react at 30-35° for 3 hr. Excess methanol was removed at 30-35° and the crude product was recrystallized from hexane as small white plates, m.p. 100.3-100.8°, 5.9 g., 92 2%.

Anal. Calcd. for $C_{12}H_{11}Cl_2NO_5$: C, 40.75; H, 2.46; Cl, 32.80; N, 4.32. Found: C, 41.00; H, 2.80; Cl, 32.65; N, 4.26.

3-(3,4-Dichlorophenyl)thiazolidinetrione (VIII).—Oxalyl chloride (12.7 g., 0.1 mole) was added dropwise to a solution of isopropyl 3,4-dichlorothionocarbanilate (26.4 g., 0.1 mole) in 50 ml. of toluene. The reaction was exothermic and HCl was evolved. After stirring for 1 hr., the solution was stirred into 250 ml. of hexane, precipitating the product. Fine white granules crystallized from toluene, m.p. 179.9-180.5°, 24.0 g., 91.6%.

Anal. Calcd. for $C_9H_3Cl_2NO_3S$ (276.1): C, 39.20; H, 1.09; Cl, 25.70; N, 5.08; S, 11.60. Found: C, 39.15; H, 1.25; Cl, 25.80; N, 5.15; S, 11.55.

The compound was also obtained on treating methyl or ethyl 3,4-dichlorothionocarbanilate with oxalyl chloride as above. Infrared and n.m.r. data are identical.

3-(3,4-Dichlorophenyl)thiazolidinedione-2-trione (XIII).—A solution of methyl 3,4-dichlorodithiocarbanilate (18.8 g., 0.075 mole) and oxalyl chloride (10.0 g., 0.08 mole) in 100 ml. of xylene was refluxed for 24 hr. HCl was evolved and a brilliant yellow color developed. Toluene was removed under vacuum at 50° leaving a gummy orange solid. Recrystallization from benzene gave bright orange needles, m.p. 150.5-151.2°, 16.0 g., 72.5%.

Anal. Calcd. for $C_9H_3Cl_2NO_2S_2$ (292.1): C, 37.10; H, 1.03; Cl, 24.30; N, 4.80; S, 21.90. Found: C, 37.15; H, 1.37; Cl, 24.35; N, 4.89; S, 21.52.

The Synthesis of Oxetane-d_6

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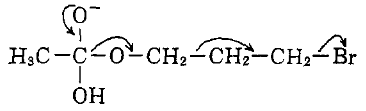
The far-infrared spectrum of oxetane (trimethylene oxide) is of value in connection with the structure of this and related four-membered ring molecules. To assist in the interpretation of the far-infrared results, it became necessary to prepare oxetane-d_6. We have synthesized this derivative and report its preparation here. The spectroscopic studies are reported elsewhere.[2]

Oxetane has been prepared previously by several routes, all starting with 1,3-propanediol.[3-9] Most of these involve three steps and give a low final yield. Further, impurities are formed in the final step which are difficult to remove from a small amount of volatile product. In this work a two-step synthesis has been used which is a modification of those of Derrick and Bissell[4] and Searles.[6] It consists of treatment of 1,3-propanediol with acetyl bromide to form γ-bromopropyl acetate, which is then converted to oxetane with strong base.

The starting material, 1,3-propane-d_6-diol, was prepared from diethyl malonate-d_2 and lithium aluminum deuteride. Deuteration of diethyl malonate with deuterium oxide containing sodium carbonate was more than 98% complete after 4 days at room temperature. The heavy glycol was converted to γ-bromopropyl-d_6 acetate by treatment with *freshly distilled* acetyl bromide. The acyl bromide was used because direct conversion to the acetate derivative[4] made unnecessary the isolation of the usual halohydrin intermediate,[5] and by employing the bromohydrin rather than the usual chlorohydrin, separation of allyl chloride (b.p. 47°, oxetane b.p. 48°) from oxetane-d_6 was avoided. The unsaturated chloride is formed as a dehydration by-product during the final step of the synthesis.

Ring closure was effected under conditions similar to those of Searles, *et al.*[7] In addition to the desired oxetane-d_6, however, a second volatile product was trapped from the reaction mixture and identified spectroscopically as ethylene-d_4. Ethylene has not been previously isolated during the preparation of oxetane and represents the simplest possible example of a 1-3 cleavage reaction. This type of elimination had been earlier observed to occur during formation of substituted oxetanes by the intramolecular Williamson reaction. Thus, during the preparation of 2,2-dimethyloxetane from 3-bromo-2,2-dimethyl-1-propanol[10] and during the preparation of 1-methyl-3-ethyloxetane from 2-chloro-4-hexanol,[11] considerable quantities of isobutylene and propylene respectively have been obtained.



$$H_3C-\underset{OH}{\overset{O^-}{C}}-O-CH_2-CH_2-CH_2-Br$$

Complete separation of the olefin from the less volatile cyclic ether was accomplished by repeated low-temperature trap-to-trap distillations. The isotopic purity of the final product was 98.8% as determined by mass spectrometry, and by-product contamination was less than 0.1% as judged by vapor phase chromatographic analysis.

Experimental

Deuterium Exchange of Diethyl Malonate with Deuterium Oxide.—All operations were carried out under anhydrous atmospheric conditions and all glass apparatus was dried at 140° for at least 10 hr. before use. To 100 g. (0.63 mole) of diethyl malonate was added a solution of 3 g. (0.03 mole) of sodium carbonate (dried at 140°) dissolved in 100 g. (5 moles) of deuterium oxide. The flask was sealed and then stirred for a 24-hr. period. At the end of that time the flask was opened and the organic phase was separated from the aqueous phase. The above procedure was repeated three times with 100-g. portions of deuterium oxide containing 3 g. of sodium carbonate in each exchange. Following the fourth exchange the ester was washed with three 10-ml. portions of deuterium oxide and dried over anhydrous magnesium sulfate. The yield of diethyl malonate-d_2 was 51 g. (50%).

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Isotopic analysis by mass spectrometry proved to be difficult, as the sample underwent back exchange while in the ion source. Rapid analysis indicated that the product consisted of 94 ± 2% diethyl malonate-d_2, 6 ± 2% diethyl malonate-d_1, and 0 ± 2% diethyl malonate, though the actual per cent of diethyl malonate-d_2 was probably somewhat higher than these figures imply.

Reduction of Diethyl Malonate-d_2 with Lithium Aluminum Deuteride.—Lithium aluminum deuteride (6.6 g., 0.157 mole) was transferred under anhydrous atmospheric conditions to a 500-ml. three-necked flask containing 250 ml. of ethyl ether freshly distilled from lithium aluminum hydride. The flask was sealed and the deuteride slurry was stirred overnight. In a nitrogen atmosphere a solution of 21.6 g. (0.133 mole) of diethyl malonate-d_2 in 30 ml. of ethyl ether (dried as above) was slowly added during a 1.5-hr. period to the lithium aluminum deuteride slurry. After refluxing for 48 hr. in an inert atmosphere, 50 ml. of deuterium oxide was cautiously added to the cooled reaction mixture. The heterogeneous system was refluxed for an additional 2 hr. and then filtered. The residue from the filtration was continuously extracted for 18 hr. with tetrahydrofuran. The organic extracts were combined and the solvents were removed *in vacuo*. The product, isolated by distillation employing a semimicro spinning band column, b.p. 95–96° (4.5 mm.), was obtained in 54% yield (6.48 g.).

Reaction of 1,3-Propane-d_6-diol with Acetyl Bromide.[12]—Acetyl bromide (Eastman White Label) was slowly distilled through a 4-in. Vigreux column. A fraction, boiling at 77° (17.5 g., 0.12 mole), was collected directly in a receiver containing 10.5 g. (0.13 mole) of 1,3-propane-d_6-diol. The temperature of the reaction mixture was maintained at 0° during the introduction of the bromide. Following the distillation, the receiver was disconnected, stoppered, and left overnight at room temperature. The flask was attached to a reflux condenser and warmed for 1 hr. at 100°. The reaction mixture was roughly divided into two fractions (1, 6.9 g., b.p. 30–60° at 19 mm.; and 2, 20.4 g., b.p. 60–74° at 19 mm.) by distillation *in vacuo*. The initial fraction was discarded. The second portion was warmed with 5 ml. of acetyl chloride for 3 hr. on the steam bath. After removal of the excess reagent by evaporation *in vacuo*, the residue was washed and dried. Distillation through a semimicro spinning-band column afforded 16.3 g. of γ-bromopropyl-d_6 acetate as a colorless liquid, b.p. 89–90° (25 mm.), 67% yield.

Reaction of γ-Bromopropyl-d_6 Acetate with Sodium and Potassium Hydroxide.[7]—γ-Bromopropyl-d_6 acetate (30.5 g., 0.16 mole) was added dropwise but rapidly (20 min.) to a well-stirred (liquid) mixture of sodium hydroxide (25 g.), potassium hydroxide (25 g.) and water (2 g.) which was maintained at a temperature of 160–170°. The volatile products were conducted through a 40-cm. Vigreux column into a Dry Ice cold trap containing sodium hydroxide pellets and finally into a liquid nitrogen cold trap. Both traps were sealed and disconnected from the system 5 min. after the last addition of γ-bromopropyl-d_6 acetate to the reaction mixture. Infrared analysis indicated that the liquid nitrogen trap contained nearly pure ethylene-d_4. The Dry Ice cold trap contained all of the oxetane-d_6 produced, together with some dissolved ethylene-d_4. The olefinic by-product was quantitatively separated from the cyclic ether by repeated low-temperature equilibrations. One trap containing the impure oxetane-d_6 was kept at −125 to −135° in a normal pentane bath; the second trap was kept at liquid nitrogen temperatures. The purified ethylene-d_4 obtained from the residues of the Dry Ice trap was subsequently combined with the material which had been originally obtained from the liquid nitrogen cold trap to give 235 mg. (4.6% yield). Final traces of water were removed from the oxetane-d_6 by treatment with fused sodium hydroxide yielding 4.68 g. (46% yield).

Vapor phase chromatography indicated a sample purity of at least 99.9%. With a column of nitromethylpimelonitrile at 27°, a retention time of 14.22 min. was observed for oxetane-d_6, whereas a value of 13.38 min. was recorded for oxetane. The isotopic content of the product was found to be 98.8 atom % D by mass spectrometry.

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Use of Cation-Exchange Resins in Organic Reactions. II. C-Acylation of Phenols

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A number of methods are available for the preparation of hydroxy aromatic ketones such as the Friedel–Crafts, the Houben–Hoesch, and the Fries reactions, or modifications of these. In the case of phenols with two hydroxyl groups *meta* to each other it was found[1,2] that, by heating the appropriate dihydric phenol with an acid anhydride in the presence of 1 drop of concentrated sulfuric acid, good yields of the corresponding hydroxy aromatic ketone were obtained. Since it was shown in part I[3] that cation-exchange resins (sulfonic acid type) were effective in bringing about the von Pechmann reaction, it was decided to use such resins as catalysts in the C-acylation of certain phenols and this paper shows that in this way good yields of ketones can be obtained from 1,3-dihydroxybenzenes.

The cation-exchange resin used was Amberlite IR-120 although Zeokarb 225 was found to be as effective. These resins were found to be stable at the temperatures used, *viz.*, for periods of 1 hr. or more at about 160–170°. The method consists essentially in heating together equimolecular quantities of phenol and acid (or acid anhydride) with an appropriate amount of cation exchange resin at 160° for a certain period of time depending on the nature of the phenol and the acid (or anhydride). The results are summarized in Table I. It should be noted that the phenols giving the best yields of ketone are resorcinol and pyrogallol whereas orcinol and hydroquinone gave the poorest yields. The yields obtained with the carboxylic acids were not much different from those using the corresponding acid anhydrides. Phenol, catechol, 3,5-xylenol, β-naphthol, 4-chlororesorcinol, and *m*-methoxyphenol were unreactive as were formic acid and monochloroacetic acid. The aromatic acids and their anhydrides gave lower yields than the aliphatic ones and did not react at all with phloroglucinol, orcinol, and hydroquinone. Although it has been shown[2] that by using an excess of concentrated sulfuric acid and twice the molecular quantity of acid anhydride diketones were formed in good yield, such compounds were not isolated using even large amounts of cation-exchange resin. For comparison a number of hydroxy ketones were prepared by the sulfuric acid method of Israelstam and Stephen[1] including a number of ketones not previously prepared by them (see Experimental). In addition it was shown that, when equimolecular quantities of resorcinol and acetic acid were heated with half the molecular quantity of concentrated sulfuric acid, a 36% yield of resacetophenone was obtained.

As in the case of the interaction of orcinol and an acid anhydride in the presence of sulfuric acid,[2] the

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