points with racemic, 2,6-dimethylcyclohexanecarboxylic acid all melted above 76.5°.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.20; H, 10.30. Found: C, 69.21; H, 10.40.

Also, VI was decarboxylated to give ethyl 2,6-dimethylcyclohex-3-ene-1-carboxylate, b.p. 65–68°/4.5 mm., n_D^{25} 1.4618.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.47; H, 9.96. Found: C, 72.37; H, 9.68.

This ester was saponified, and the acid produced was hydrogenated to give a saturated acid, m.p. 70–71°, which had the composition of V. A mixture with racemic 2,6-dimethylcyclohexanecarboxylic acid gave a higher melting point.

Esterification of II. Equimolar amounts of diazomethane and II in ether at room temperature for 2 hr. gave 79% methyl 2,6-dimethyl-3-cyclohexene-1-carboxylate-1-carboxylic acid, m.p. after recrystallization from formic acid, 145–145.5°.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.23; H, 7.60. Found: C, 62.03; H, 7.82.

Esterification with excess diazomethane gave diester, m.p. 72–73° after recrystallization.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.73; H, 8.02. Found: C, 63.79; H, 8.17.

2,6-Dimethyl-3-cyclohexene-1,1-dicarboxylic hydrazide. To 6.0 g. (0.024 mole) of I was added a solution of 2.0 g. (0.083 g.-atom) of sodium in 1.9 g. (0.059 mole) of 95% hydrazine and 50 ml. of anhydrous ethanol. The yellow solution was stirred and refluxed for 6 hr., then cooled in ice. A precipitate formed but dissolved when 100 ml. of water was added. A yellow oil separated and was taken up in petroleum ether. The petroleum ether solution was concentrated and 0.9 g. of I was recovered. The water solution was acidified cold and extracted with ether. The etheral extract was dried, the solvent was removed, and the residue recrystallized from ether. The crystals, m.p. 191–194°, gave a positive test for nitrogen; yield 56%.

Anal. Calcd. for $C_{10}H_{14}O_2N_2$: C, 62.34; H, 7.27. Found: C, 62.06; H, 7.10.

Crotonic acid and trans-1,3-pentadiene. A solution of 8.6 g. (0.10 mole) of crotonic acid, 12.2 g. (0.18 mole) of 1,3-pentadiene, and a few crystals of hydroquinone were sealed under nitrogen in a heavy-walled Pyrex glass tube and heated at 180° for 2 hr. (Meek heated for 8 hr. at 200–230°). When cooled the tube contained a viscous oil that soon deposited crystals. Petroleum ether was added, and the solution soon deposited 8 g. of crystals. These were recrystallized from petroleum ether to give 4 g. (26%) of colorless crystals, m.p. 85.5–87°. These were hydrogenated in methanol over Adams' catalyst to a colorless solid, m.p. 73–78°, equivalent weight 155.8 (calcd. for $C_9H_{16}O_2$; 156.2). Several recrystallizations of the acid from 1.67 g. of adduct gave 0.20 g. of meso *trans*-2,6-dimethylcyclohexanecarboxylic acid, m.p. 103–104° (no m.p. depression in mixture with authentic meso *trans* acid).

Ethyl crotonate and trans-1,3-pentadiene. The procedure was like that used for ethylidenemalonic ester (12 hr., 170–180°). The product was fractionally distilled through a center rod column. Redistillation of a center cut, b.p. 85–86°/11 mm. (15 g.) gave several fractions; a portion with b.p. 87–88.5°/11 mm. was analyzed.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.47; H, 9.96. Found: C, 72.36; H, 10.21.

Yields were low because considerable polymerization occurred and because separation from other products was difficult.

Saponification of the ester and recrystallization of the acid from ethyl acetate gave an 83% yield of material, m.p. 83–85°.

LOS ANGELES, CALIF.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

Bicyclic Ortho Esters by Direct Esterification

RODERICK A. BARNES, GERALD DOYLE,[1] AND JOSEPH A. HOFFMAN[2]

Received August 17, 1961

The stronger organic acids, such as 3,5-dinitrobenzoic acid and di- and trichloroacetic acids, have been found to react directly with a 2-hydroxymethyl-2-methyl-1,3-propanediol to yield bicyclic ortho esters.

Ortho esters usually have been prepared from a nitrile which is converted first to the imino ester hydrochloride and this latter substance then is heated with an alcohol.[3] Bicyclic esters related to the present work have been previously prepared by an ester interchange involving a triol and a noncyclic ortho ester.[4,5]

The successful preparation of bicyclic phosphites and phosphates[6] from 2-hydroxymethyl-2-alkyl-1,3-propanediols led us to attempt similar preparations in the carbon series. The first approach, analogous to that used for the preparation of a phosphite, employed benzotrichloride, 2-hydroxymethyl-2-methyl-1,3-propanediol (I), and triethylamine. The only product isolated was tetrachlorodibenzyl (II). An attempt to promote SN1 reactions of benzotrichloride by using silver carbonate in the reaction mixture also failed and II was isolated again. Com-

(1) The major part of this work was taken from a thesis presented by Gerald Doyle for the B.S. degree, as a part of the Henry Rutgers Scholars program, May 1961.

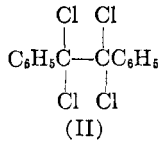
(2) The first successful preparation of an ortho ester was described in a thesis presented by J. A. Hoffmann to the Graduate School for the Ph.D. degree, December 1958.

(3) S. M. McElvain and J. W. Nelson, *J. Am. Chem. Soc.*, **64**, 1825 (1942).

(4) E. Stetter and K. H. Steinacker, *Chem. Ber.*, **85**, 451 (1952), treated *cis*-phloroglucitol with ethyl γ,γ,γ-triethoxypropionate.

(5) W. E. Doering and L. K. Levy, *J. Am. Chem. Soc.*, **77**, 509 (1955), allowed 2-hydroxymethyl-2-methyl-1,3-propanediol to react with ethyl orthoformate.

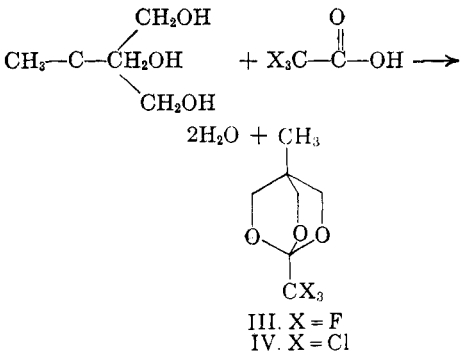
(6) Our results with the phosphorus esters were generally similar to those which have been reported independently by J. G. Verkade and L. T. Reynolds, *J. Org. Chem.*, **25**, 663 (1960) and by W. S. Wadsworth and W. D. Emmons, Abstracts 138th Meeting, ACS, New York, p. 97P.



(II)

pound II has been observed to result from benzotrichloride under a variety of experimental conditions.[7] A reasonable assumption is that phenyldichloromethyl radicals are intermediates in the formation of II.

The direct preparation of an ortho ester from triol I and several acids was next attempted. It seemed possible that the same factors which make the preparation of a ketal from ethylene glycol successful whereas simple alcohols fail, could also operate in this situation.[8] The realization of this possibility was first achieved[2] by using trifluoroacetic acid and triol I. The water generated during the reaction was removed continuously by azeotropic distillation with benzene.



III. X = F
IV. X = Cl

Attempts to use this method for other acids were not successful until xylene was used to replace benzene as the solvent and to drive out the water. In this way it was possible to prepare the ortho ester of several α-halogenated acids. Attempts to use solvents boiling above 150° failed because at this temperature triol I begins to decompose with elimination of water to produce dark colored substances.

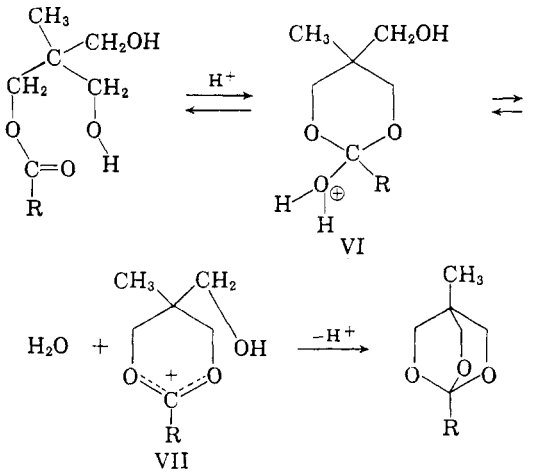
Although benzoic acid itself yielded only mixtures of ordinary esters, 3,5-dinitrobenzoic acid did furnish the desired ortho ester in low yield. There appears to be some correlation between the ionization constant of the acid and the yield of ortho ester (Table I).

TABLE I

Acid	K_a	Yield of Ortho Ester, %
Trifluoroacetic		51
Trichloroacetic	1.2	41
Dichloroacetic	5.1×10^{-2}	40
α,α'-Dichloropropionic	3.3×10^{-2}	29
o-Nitrobenzoic	6.4×10^{-3}	0
3,5-Dinitrobenzoic	1.5×10^{-3}	4
Chloroacetic	1.5×10^{-3}	0
Nicotinic	1.9×10^{-5}	0
Caproic	1.4×10^{-5}	0
Benzoic	6.3×10^{-6}	0

The yields in Table I represent ortho ester actually isolated and it is quite possible that small amounts of ortho ester were formed in some cases but were not separable from the larger amounts of mono-, di-, and triesters of triol I. With nicotinic acid a crystalline product was isolated but this proved to be the dinicotinate ester of I.

The difference in behavior of acids having electron attracting groups from other acids might result either because of differences in equilibria or in rates. Although the experimental data is certainly not adequate to define the mechanism, a large difference in rates is believed to be responsible for the experimental observations. The argument is based on the assumption that if equilibrium were actually achieved, the azeotropic removal of water would shift the equilibrium so that ortho ester would result from all acids.



When R is a strongly electron-attracting group the concentration of intermediate VI would be increased.[9] The relative rate of reaction of VII with water to regenerate VI as compared to the rate of

(7) Pyrolysis, catalytic reduction, and heating with copper powder have all converted benzotrichloride to II. See W. Loeb, *Ber.*, **36**, 3060 (1903); W. Borsche and G. Heimburger, *Ber.*, **48**, 458 (1915), and P. Karrer *et al.*, *Helv. Chim. Acta*, **11**, 235 (1928).

(8) Although thermodynamic data are not available, we believe that the change in the number of particles during the reaction, which is manifested by a change in the entropy part of the free energy change, may account for the success of the reactions to form cyclic and bicyclic products. The formation of an ortho ester from methanol would require that four molecules of starting materials combine to yield three molecules of products while with triol I two molecules of starting materials generate three molecules of products.

(9) This should be analogous to the reaction of chloral with water to form the hydrate. The unfavorable charge distribution resulting from having the trihalomethyl group with its positive carbon joined directly to the positive carbon of the aldehyde group is ameliorated by adding water to the carbonyl group. Thus, chloral is completely hydrated while ordinary aldehydes form hydrates to some extent only in water solution.

cyclization to product may be critical. Intermediate VII, with the positive charge distributed over the two oxygens and the carbon, may be so stable that it reacts at an appreciable rate only with water to regenerate VI. However, an electron-attracting R group could inductively increase the positive charge on the carbon atom of VII and in this way facilitate attack by bases, in particular by the third hydroxyl group of I to yield the ortho ester.

Since the conversion of α,α'-dihalo acids to ortho esters is most likely a general reaction, subsequent hydrogenolysis of the halogens would provide a general route for the preparation of ortho esters in which R = CH_2R'. This scheme was tested by reducing ortho ester IV with hydrogen and Raney nickel in alcoholic potassium hydroxide solution. A rather low yield of the desired halogen-free ortho ester was isolated (R = CH_3). This product, when freshly sublimed, had no carbonyl or hydroxyl bands in its infrared spectrum. However, prolonged standing in air resulted in decomposition to a viscous liquid having infrared absorption bands in both the hydroxyl and carbonyl region. A similar sensitivity toward hydrolysis by water alone has been noted by Doering and Levy[5] for their ortho ester (R = H). The other orthoesters were considerably more stable.

An attempt to replace triol I by glycerol in the reaction with trichloroacetic acid did not yield an isolable amount of ortho ester. The expected ring system, 2,6,7-trioxabicyclo[2.2.1]heptane, by analogy with the carbon system, would be expected to have considerably more strain[10] and hence would be less readily formed than the 2,6,7-trioxabicyclo-[2.2.2]octane system.

EXPERIMENTAL[11]

Reaction of benzotrichloride with triol I. A mixture of benzotrichloride (9.8 g.), triethylamine (31.0 g.), triol I (6.0 g.), and dioxane (500 ml.) was refluxed for 48 hr. Triethylamine hydrochloride (7 g.) was filtered and the solvents were distilled. The residue was dissolved in ether and washed with water. Evaporation of the ether left a dark oil which partly crystallized. Recrystallization from benzene-ligroin produced 2.0 g. (25%) of tetrachlorodibenzyl (II) which melted at 159–160°.

Anal. Calcd. for $C_{14}H_{10}Cl_4$: C, 52.54; H, 3.15; Cl, 44.3. Found: C, 52.55; H, 3.21; Cl, 43.53.

A similar experiment using silver carbonate (52 g.) in place of triethylamine yielded only II. Omission of the triol from the reaction mixture also produced II in approximately the same yield.

4-Methyl-1-trifluoromethyl-2,6,7-trioxabicyclo[2.2.2]octane (III). A mixture of trifluoroacetic acid (6 g.), triol I (6 g.) and sulfuric acid (3 drops) was heated at 100°. After 12 hr. a considerable portion of the product had sublimed from the reaction mixture. The heating was continued as long as any sublimate continued to be formed (*ca.* 48 hr.). The combined material (6.5 g., 51%) was recrystallized from hexane, m.p. 144–145°. The infrared spectrum had no bands in either the hydroxyl or carbonyl region.

Anal. Calcd. for $C_7H_9O_3F_3$: C, 43.43; H, 4.58. Found: C, 42.58; H, 4.75. Mol. wt., 194. (Calc. mol. wt., 198.)

The sulfuric acid catalyst was found to be unnecessary and, furthermore, there was no darkening of the reaction mixture when it was omitted.

1-Methyl-4-trichloromethyl-3,5,8-trioxabicyclo[2.2.]octane (IV). Trichloroacetic acid (81 g.), triol I (60 g.), *p*-toluenesulfonic acid (6 g.) and xylene (400 ml.) were refluxed using a Dean-Starke trap to remove water formed during the reaction. After 12–15 hr. 16 ml. (90%) of water had been collected. When the reaction mixture was chilled, a crystalline precipitate was formed (33 g.). Both the precipitate and the filtrate were washed with sodium carbonate solution to neutralize the acid catalyst. Evaporation of the filtrate yielded additional product. Recrystallization from benzene finally yielded 51 g. (41%) of ortho ester XIIb which melted at 218–221° (sealed cap). The infrared spectrum of this product was very similar to that of III.

Anal. Calcd. for $C_7H_9O_3Cl_3$: C, 33.96; H, 3.67. Found: C, 34.21; H, 3.77.

The other ortho esters were prepared in a similar manner. Triol I (24 g.) when allowed to react with dichloroactic acid (25.6 g.) yielded 17 g. (40%) of *1-dichloromethyl-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane*, m.p. 138–139° after recrystallization from benzene.

Anal. Calcd. for $C_7H_{10}O_3Cl_2$: C, 39.46; H, 4.73. Found: C, 39.53; H, 4.68.

α,α'-Dichloropropionic acid (25 g.) and I (21.8 g.) yielded 11.3 g. (29%) of *1-(1,1-dichloroethyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane* which melted at 151–153° after recrystallization from benzene. The analysis of this compound indicated that it had absorbed some water.

Anal. Calcd. for $C_8H_{12}O_3Cl_2$: C, 42.31; H, 4.33; Cl, 31.23. Calcd. for $C_8H_{12}O_3Cl_2 \cdot {}^1/_6\ H_2O$: C, 41.90; H, 5.38; Cl, 30.92. Found: C, 41.66; H, 5.22; Cl, 30.74.

From 3,5-dinitrobenzoic acid (42 g.) and I (24 g.) there was obtained by cooling the reaction flask, some yellow crystalline material, m.p. 109–112°. This substance was not further identified since its infrared spectrum had hydroxyl and carbonyl bands. Concentration of the filtrate yielded a white product (2.4 g.). Recrystallization from benzene produced pure *1-(3,5-dinitrophenyl)-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane* (2 g., 4%) which melted at 224–225°.

Anal. Calcd. for $C_{11}H_{12}O_7N_2$: C, 48.65; H, 4.08. Found: C, 48.66; H, 4.25.

The unsuccessful experiments were processed by chilling the reaction mixture. If no crystals appeared, the solution was washed with sodium bicarbonate solution to remove acids and then the solvent was removed. Since the bicyclic ortho ester would almost certainly be the most volatile component, distillation and, or sublimation of the residual material was attempted. The infrared spectra of any substance obtained in this manner was examined for indications that an ortho ester was present.

Dinicotinate of triol I. Nicotinic acid (24.8 g.) and I (24 g.) were allowed to react as in the preparation of ortho esters. When the warm reaction mixture was cooled to room temperature a yellow oil separated and then hardened to an intractible glass. When the xylene solution was washed with potassium carbonate solution and refrigerated for several hours, a small amount of a white crystalline product separated, m.p. 119–120°.

Anal. Calcd. for $C_{17}H_{18}O_5N_2$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.96; H, 5.68; N, 8.46.

This substance had strong absorption in the carbonyl region and a rather weak hydroxyl band.

Reduction of ortho ester IV. Ortho ester IV (15 g.) was added to a solution of potassium hydroxide (20 g.) in absolute ethanol (300 ml.). Raney nickel (5 g.) was added and the

(10) P. D. Bartlett and J. Bank, *J. Am. Chem. Soc.*, **83**, 2591 (1961) have estimated the strain in norbornene to be 19 kcal. per mole. The strain in the bicyclo[2.2.2]octane system may be as high as 9 kcal.; see P. R. Schleyer and R. D. Nicholas, *J. Am. Chem. Soc.*, **83**, 2700 (1961).

(11) Melting points were determined using the Kofler hot-stage. Analyses were by W. Manser, Zurich, Switzerland, and G. Robertson, Florham Park, N. J.

mixture shaken at room temperature with hydrogen at 50 p.s.i. The theoretical amount of hydrogen was absorbed in about three days. Anhydrous magnesium sulfate was added to the reaction mixture and the solids were filtered. Dry benzene was added to the filtrate and the solution was concentrated; the last 50 ml. was removed at reduced pressure. Only a part of the total residue could be sublimed as a white crystalline substance. After two additional sublimations the product, 1,4 - dimethyl - 2,6,7 - trioxabicyclo[2.2.2]octane melted at 85–90°. This substance absorbed water rather quickly from the atmosphere to become a colorless viscous liquid. Even careful handling prior to analysis permitted the absorption of considerable water.

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Calcd. for $C_7H_{12}O_3 \cdot {}^1/_2\,H_2O$: C, 54.89; H, 8.55. Found: C, 54.81, 54.94; H, 8.12, 8.31.

The reaction of trichloroacetic acid with glycerol. A mixture of trichloroacetic acid (33 g.), glycerol (18.4 g.), *p*-toluenesulfonic acid (2 g.), and xylene (350 ml.) was refluxed for 24 hr. with evolution of 6 ml. of water (two equivalents is 7.2 ml.). The solution was cooled, washed with sodium bicarbonate, and concentrated. The first fractions obtained on vacuum distillation boiled at 125–135°/3 mm. The infrared spectra of these fractions had strong carbonyl and hydroxyl absorption bands.

NEW BRUNSWICK, N. J.

[COMMUNICATION NO. 2205 FROM THE KODAK RESEARCH LABORATORIES, EASTMAN KODAK COMPANY]

Preparation of Thiols

B. C. COSSAR, JANE O. FOURNIER, D. L. FIELDS, AND D. D. REYNOLDS

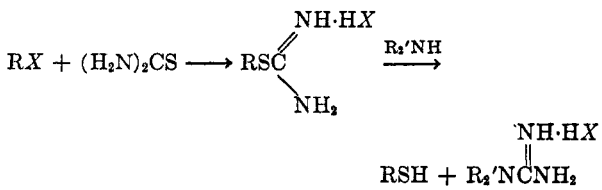
Received June 29, 1961

An improved method of preparing simple thiols is described. The steps involved are (1) preparation of an isothiuronium salt in a high-boiling solvent, followed by (2) cleavage of this salt with a high-boiling amine. The desired thiol is separated by distillation, leaving a guanidine salt by-product as residue. The process is not applicable to the preparation of 1,2-ethanedithiol. It is prepared by an alternate procedure involving the reaction of ethyl 2-mercaptoethylcarbonate with ammonium hydrosulfide.

During the one hundred twenty-five years since the discovery of the first mercaptan or thiol, preparation of the lower members has been unpleasant because of their inherent odors. The need for a variety of mono- and dithiols prompted a search for a more satisfactory method of preparation.

The method involving the action of aqueous alkali on isothiuronium salts has superseded most of the others used for laboratory-scale preparations.[1] Isolation usually involves either a steam distillation or an ether extraction, and in some instances both. During recent mercaptoethylation studies[2] an amine was used to cleave an isothiuronium salt to generate a thiol *in situ*. A similar reaction has been used by others for the synthesis of substituted guanidines[3] and for the preparation of mercaptoalkanesulfonic acids.[4] This type of reaction has now been adapted to the preparation of mono- and dithiols by a general method which eliminates handling operations.

The steps involved are the preparation of an isothiuronium salt in a high-boiling solvent, followed by cleavage of this salt by a high-boiling strong amine. The products are the desired thiol and a nonvolatile guanidine salt.



The solvent and the amine should be chosen so that their boiling points are well above that of the thiol being prepared. Triethylene glycol and tetraethylenepentamine have been used in the present study because of their low cost and ready availability. The over-all time required for a one-mole run is approximately one hour. The products prepared are listed in Tables I and II.

TABLE I

THIOLS

RSH

R	B.P.	n_D^{25}	Purity, %	Yield, %
C_2H_5—	35	1.4269	99.7	68
n-C_3H_7—	65	1.4345	98.5	79
n-C_4H_9—	96–97	1.4407	99.5	77
n-C_6H_{11}—	123–124	1.4439	100.0	75
n-C_7H_{17}—	91–93/24 mm.	1.4518	97.7	84
n-$C_{10}H_{21}$—	94/5 mm.	1.4545	100.0	87

It was of interest to find that this synthesis could not be adapted to the preparation of 1,2-ethanedithiol. When the isothiuronium salt prepared from 1,2-dibromoethane was cleaved with tetraethylenepentamine, no product distilled below the boiling

(1) E. E. Reid, *Organic Chemistry of Bivalent Sulfur*, Vol. I, Chemical Publishing Co., Inc., New York, 1958, p. 32.

(2) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, 26, 5116 (1961).

(3) M. Schenk and H. Kerchhof, *Z. physiol. Chem.*, 158, 90 (1926); R. Phillips and H. T. Clark, *J. Am. Chem. Soc.*, 45, 1755 (1923).

(4) C. Schramm, H. Lemaire, and R. Karlson, *J. Am. Chem. Soc.*, 77, 6231 (1955).