6-*O*-Acetyl-5-*S*-acetyl-3-*O*-benzoyl-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (6).—A mixture of **5** (34 mg) and potassium acetate (300 mg) in 5 ml of acetic acid–acetic anhydride (1:5, v/v) was heated at 140°. After 16 hr, the reaction mixture was coevaporated with toluene to dryness, extracted with ether, and concentrated. The crystalline product was purified by column chromatography on silica gel, using ether–hexane (2:3, v/v) as eluent to give **6** (440 mg, 96.7%), mp 129–30°, $[\alpha]^{25}D$ −80.8° (*c* 0.5, chloroform).

Anal. Calcd for $C_{20}H_{24}O_8S$: C, 56.57; H, 5.69; S, 7.55. Found: C, 56.75; H, 5.83; S, 7.50.

Reaction of 6 with Sodium Methoxide.—Compound **6** (100 mg) was dissolved in anhydrous methanol (10 ml) and cooled to 0°. A solution of sodium methoxide in methanol was added and the pH was adjusted to 10. Progress of the reaction was monitored by tlc using ether–hexane (2:3, v/v) as the irrigant. After 1 hr, the reaction mixture was neutralized with Amberlit IR-120 (H^+) resin, evaporated, and chromatographed on alumina with ether–hexane (1:10, v/v) to give **7** (40 mg, 77.81 %).

Registry No.—**1**, 37614-73-6; **2**, 37614-74-7; **3**, 37614-75-8; **4**, 37614-76-9; **5**, 37614-77-0; **6**, 37614-78-1; **7**, 37614-79-2; **8**, 10227-17-5; **9**, 10227-18-6.

Protection of Carbonyl Groups as Bromomethylethylene Ketals

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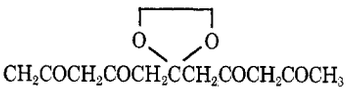
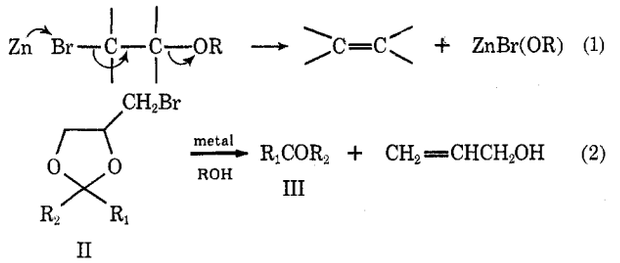
Received October 2, 1972

Ketalization has proven to be an invaluable method for the protection of a carbonyl group during various transformations. However, a ketal protecting group necessitates the use of acid catalysis for its removal. During the course of studies directed toward a total synthesis of the spiro alkaloid histrionicotoxin,[1] a carbonyl protecting group which could be removed under neutral conditions was required. Other instances of the inadequacy of conventional methods for carbonyl protection have been noted previously; *e.g.*, removal of the ketal blocking group from the polyketide I could not be achieved.[2]



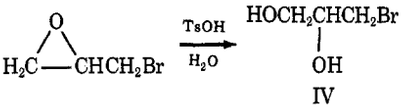
I

A promising approach seemed to be the use of a bromomethylethylene ketal which could be cleaved by the familiar β-bromo ether reductive elimination (eq 1; *cf.* ref 3). More specifically, the simplest cyclic ethylene ketal (II) was selected for use, the unmasking step then being expressed by eq 2.



II

Following the procedure of Winstein and Goodman, the requisite starting material, 1,2-dihydroxy-3-bromopropane[4] (IV), was prepared in one step from epibromohydrin. Three substrates, V–VII, were chosen to



IV

illustrate the generality of the sequence ketalization–deketalization. The first step, ketalization, was accomplished in excellent yield by treatment of an aldehyde or ketone with bromoglycol IV in refluxing benzene using *p*-toluenesulfonic acid as a catalyst (Table I). Deketalization was attempted using a variety of

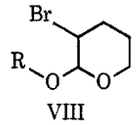
TABLE I

Carbonyl compd	Yield of Ketal,[a,b] %	Yield of deketalized material,[a,c] %
4-*tert*-Butylcyclohexanone (V)	98[d]	89
$CH_3(CH_2)_4COCH_2COOCH_3$ (VI)	95[e]	96
$CH_3(CH_2)_{10}CHO$ (VII)	93[f]	89

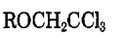
[a] Evaporatively distilled. [b] The ketals showed the expected spectral and analytical properties. [c] Infrared and nmr spectra were identical with those of authentic material. [d] Mass spectrum M^+ calcd 290.0082, found 290.0879. [e] ($M^+ - CH_3OM$) calcd 277, found 277 (no parent ion). [f] M^+ calcd 320.1350, found 320, 1342.

metals and conditions.[3,5] After some experimentation, it was found that treatment of the bromo ketal with activated zinc in refluxing methanol afforded an excellent yield of the deketalized compound (Table I).

The bromomethylethylene ketal unit has been found to be stable to a variety of reagents which are commonly used in synthesis. Thus, treatment of the ketal obtained from 4-*tert*-butylcyclohexanone with *m*-chloroperbenzoic acid, liquid ammonia, $NaBH_4$ in ethanol at room temperature, MeLi in ether at 0° for 1 hr, or Jones (CrO_3) reagent led to a *quantitative recovery* of starting ketal. In addition, it should be noted that there are many hydroxyl, amino, and carbonyl protecting groups which can survive the deketalization conditions and only a few, for example the alcohol protecting groups VIII and IX, which cannot.



VIII



IX

Experimental Section

The following experiments illustrate the procedures utilized.

Ketalization.—Dodecanal (634 mg, 3.40 mmol) in 2 ml of benzene was added portionwise to a refluxing benzene solution (50 ml) of bromoglycol IV (5.3 g, 34.0 mmol) and *p*-toluenesulfonic acid (50 mg) over 10 hr. The solution was heated at reflux for an additional 5 hr, and the product was isolated after washing with water and removal of benzene to afford 1.10 g (100%) of crude bromo ketal. Evaporative distillation (120°,

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(5) Representative metals tried were Zn, Al–Hg, Mg–Hg, Zn–Cu, Zn–Hg, and Li–Hg.

0.08 mm) afforded 1.040 g (93%) of dodecanal bromo ketal as a colorless oil: infrared peaks (film) at 8.75 and 8.90 μ; nmr $\delta_{TMS}^{CDCl_3}$ 4.99 (HCOO, multiplet), 4.58–3.17 [OCH(CH_2Br)CH_2O, complex], and 0.89 ppm (CH_3, triplet, J = 4.0 Hz); mass spectrum calcd for $C_{15}H_{29}O_2Br$ 320.1350; found 320.1342.

Deketalization.—A solution of 162 mg (0.505 mmol) of dodecanal bromo ketal and 500 mg of zinc dust in 10 ml of methanol was heated at reflux under argon for 12 hr. The zinc was removed by filtration, and the product was isolated by ether extraction and evaporatively distilled (bp 80°, 0.07 mm), yielding 83 mg (89%) of dodecanal, identical with an authentic sample. The zinc was activated by brief treatment with acetic acid followed by washing with methanol.

The efficiency of introduction and removal of the bromomethylethylene ketal group, its stability toward many synthetic reagents, and the selectivity with which it can be removed[6] all indicate a real utility in synthesis.[7]

Registry No.—IV, 4704-77-2; V, 98-53-3; V bromo ketal, 37447-43-1; VI, 22348-95-4; VI bromo ketal, 37447-45-3; VII, 112-54-9; VII bromo ketal, 37447-47-5.

(6) For controlled potential electrolytic removal of such groups, see M. F. Semmelhack and G. E. Heinsohn, *J. Amer. Chem. Soc.*, **94**, 5140 (1972).

(7) This research was financially assisted in part by the National Institutes of Health and the National Science Foundation.

Acid Hydrolysis Products of DDD and DDT Precursors[1]

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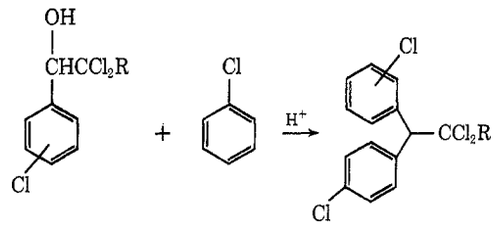
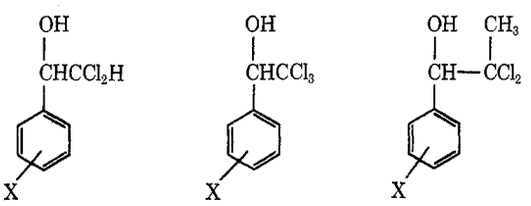
Received September 8, 1972

The widespread use of 2,2-di(*p*-chlorophenyl)-1,1,1-trichloroethane (DDT) as a pesticide as well as the more limited use of 2-(*o*-chlorophenyl)-2-(*p*-chlorophenyl)-1,1-dichloroethane (*o,p'*-DDD) as the only clinically approved agent for the treatment of adrenocortical carcinoma has prompted numerous chemical investigations in these classes of compounds.[3-13] Studies in our laboratories have been devoted to (1) preparing derivatives of *o,p'*-DDD which lack the serious toxicity of this drug and (2) studying the chemistry of the precursors used in the synthesis of these derivatives.

The conventional and most direct method for the preparation of DDD derivatives involves the acid-catalyzed condensation of 1-(chlorophenyl)-2,2-di-



chloroethanols with chlorobenzene.[3,8] This method is commonly employed, since usable amounts of DDD's are obtained from readily available starting materials. However, the yields are generally rather poor (*ca.* 30–50%).[3,8] An investigation of the products and by-products in this reaction was, therefore, undertaken to aid in delineating the scope and limitations of this reaction. Moreover, ramifications of this work can be extended to the synthesis and hydrolysis of DDT and its precursors. This paper reports the products formed when phenyldichloroethanols **1**, phenyltrichloroethanols **2**, and phenyldichloropropanols **3** are subjected to concentrated sulfuric acid,[14] conditions normally employed for the synthesis of DDT[3] and DDD.[8]



1a, X = *o*-Cl; **b**, X = *m*-Cl; **c**, X = *p*-Cl

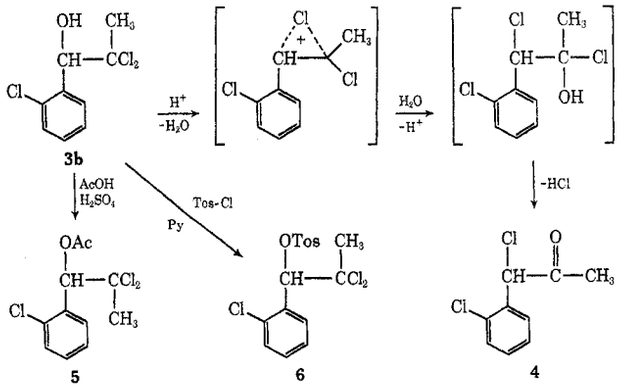
2a, X = H; **b**, X = *o*-Cl

3a, X = H; **b**, X = *o*-Cl; **c**, X = *p*-Cl

Glc–mass spectral analysis and infrared and nuclear magnetic resonance spectroscopy were employed for characterization of the products.

Results and Discussion

Unexpected results were obtained in the acid hydrolysis of the phenyldichloropropanols **3**. Treatment of 2,2-dichloro-1-(*o*-chlorophenyl)propanol (**3b**) with concentrated sulfuric acid at 40–45° for 3 hr afforded, exclusively, 1-(*o*-chlorophenyl)-1-chloropropanone (**4**). One possible means for such a conversion can be explained as proceeding through a chloronium ion as shown below.



(1) This investigation was supported by the U. S. Public Health Service under Research Grants No. CA-49340 and CA-08349 from the National Cancer Institute.

(2) (a) Department of Chemistry, University of Maine, Orono, Maine 04473; (b) National Institutes of Health Postdoctoral Fellow, 1970–1972.

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