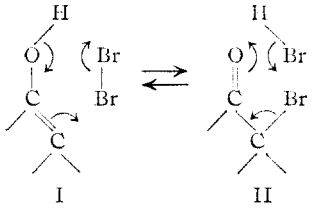
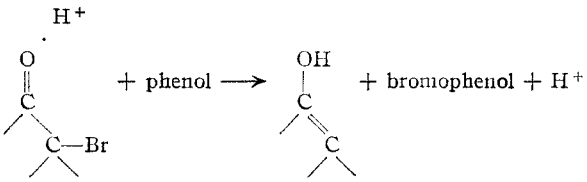


There has not been much discussion of the mechanisms of the forward and backward reactions other than the statement that the mechanism of the reduction of bromoketone must be the exact reversal of the bromination of ketone.[1d]

In studies of the reduction of bromoketones by hydrogen bromide bromine acceptors, 2-naphthol[1c] and cyclohexene,[1d] were used. We were interested to know whether free bromine was the brominating agent or a positively charged complex involving bromoketone and a proton was involved. Experiments were conducted by sealing a mixture of a bromoketone, phenol and an acid in glacial acetic solution and allowing the reactions to proceed for varying periods. At first, *p*-bromophenacyl bromide was used but this was later replaced by bromoacetomesitylene. This change was made because self-condensation side reactions involving *p*-bromoacetophenone did not occur with the hindered ketone. Furthermore, since the rate of reaction was about the same in the case of bromoacetomesitylene, any mechanism involving addition to the carbonyl group (in the usual sense) may be ruled out. These experiments indicated that the acid strength of the acid used was not the dominating factor. For example in comparable experiments using bromoacetomesitylene and hydrogen bromide or perchloric acid the yield of acetomesitylene was over 90% in the former case and of unchanged bromoacetomesitylene over 80% in the latter. This rules out the reaction sequence pictured below.



Thus it is evident in the reduction of bromoketones by hydrogen bromide that: (1) the bromine moiety of the hydrogen bromide plays a definite role; (2) the process does not involve a direct acid-catalyzed transfer of bromine from bromoketone to phenol.

From the above discussion and evidence we believe it likely that both the acid-catalyzed bromination of ketones and the reduction of bromoketones by hydrogen bromide proceed by a cyclic mechanism involving a common cyclic activated state (not pictured). This conclusion is consistent with the fact that bromination of a ketone involves the enol form.[2] However, this work does not rule out a rate controlling stepwise reduction[1d] as shown below.

$$[RCOC(R_2)Br\cdot H]^+ + Br^- \longrightarrow RCOCH(R)_2 + Br_2$$

Experimental[4]

Reduction of *p*-Bromophenacyl Bromide.—In a typical experiment a moderate stream of gaseous hydrogen bromide was bubbled into a mixture of 3.0 g. of bromoketone and 1.5 g. of phenol in 12 cc. of glacial acetic acid in an ampoule which was then sealed. This mixture containing undissolved crystals of bromoketone was shaken frequently and left at room temperature (about 25°). After three days a small amount of solid remained but after four days the mixture was homogeneous. On the fifth day the tube was opened and the products taken into ether–benzene. After washing well with water, alkali and saturated sodium chloride solution the solvents were removed and the residue distilled to yield 1.16 g. (54%) of colorless oil, b.p. about 135° at 34 mm., and a tarry residue. The distillate solidified and on crystallization from diluted alcohol there was obtained with little loss pure *p*-bromoacetophenone, m.p. and mixed m.p. with authentic material, 49.5–51.5°. The oxime, formed in 93% yield from hydroxylamine hydrochloride and pyridine, melted alone and mixed at 128–130°.

In a similar experiment except that 1.0 g. of *p*-toluenesulfonic acid replaced the hydrogen bromide, the reaction mixture remained unchanged for 49 days. On heating such a mixture to 80° for four hours, it darkened and only tar was obtained. In another experiment in which hydrogen chloride replaced the hydrogen bromide the rate of disappearance of undissolved bromoketone was much slower, 24 days being required before the mixture became homogeneous. After 37 days the mixture was processed as above to yield a smaller amount (about 20%) of *p*-bromoacetophenone.

Reduction of Bromoacetomesitylene.—In an experiment similar to the above except that 2.0 g. of bromoacetomesitylene[5] was used instead of *p*-bromoacetophenone the reaction mixture was allowed to stand for seven days. After the usual procedure there was obtained 1.87 g. (93%) of acetomesitylene, b.p. about 140° at 40 mm., $n^{25}D$ 1.5145.[6] This compound was further identified by nitration to 3,5-dinitroacetomesitylene,[7] m.p. and mixed m.p. 139–140.4°. In another experiment 2.6 g. of 60% perchloric acid was treated with a solution of 5 cc. of acetic anhydride in 5 cc. of glacial acetic acid. This solution was then added to bromoketone and phenol so that the final reaction mixture was similar to that above except for the change of acids. After standing for seven days the mixture was processed to yield 2.6 g. (86%) of unchanged starting bromoketone, m.p. and mixed m.p. 55.0–56.0°.

(4) The author is indebted to the Graduate School for providing a grant and to Mr. C. C. Cochrane for preparing some of the compounds used.

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(6) C. R. Noller and R. Adams, THIS JOURNAL, **46**, 1893 (1924), give $n^{20}D$ 1.5175.

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The Preparation of *n*-Butyl α-D-Glucoside

BY WARD PIGMAN AND R. O. LAFFRE

The new compound *n*-butyl α-D-glucoside has been prepared by a *trans*-glycosidation procedure from methyl α-D-glucopyranoside. Since relatively few α-glucosides are known, the preparation and properties of the new compound are reported.

Experimental

Preparation.—To 170 cc. of dried *n*-butanol was added 50 g. of methyl α-D-glucopyranoside, and the solution was heated to the boiling point. Then, 30 cc. of butanol (0.44 *N* with respect to HCl) was added, and the solution was refluxed for a total of 20 hours. New 20-cc. portions of the butanol–HCl were added after 7 and after 8 hours. After 9 hours, 100 cc. of the solution was removed by distillation, and 30 cc. of the butanol–HCl was added. (Hydrogen chloride is lost easily under reflux conditions.) The cooled solution was then treated with activated carbon (Darco),

filtered and concentrated *in vacuo* (water-pump) to a thick sirup. The sirup was diluted to about 250 cc. with acetone and stored at −10 to −15°. Crystallization occurred after several days; yield 5 g.

The product was recrystallized nineteen times from USP chloroform, by allowing 3% solutions to crystallize slowly at −15°.

The purified material was bitter tasting, somewhat hygroscopic, and crystallized as long fine needles which tended to form gels in most solvents. It was quite soluble at room temperature in water, alcohol, acetone, benzene, chloroform, ethyl acetate and carbon tetrachloride; it was more difficultly soluble in ether (USP). The optical rotation was $[\alpha]^{20}D$ +135.4 (H_2O, *c* 4). The capillary m.p. was 86–87°; on a heated stage using polarized light, the m.p. was 81–82°.

Anal. Calcd. for $C_{10}H_{20}O_6$: C, 50.83; H, 8.55. Found: C, 50.5, 50.4; H, 8.80, 8.89. (Analysis made by W. J. Barrett of the Southern Research Institute, Birmingham.)

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The S-Butyl Group in Alkylations. Preparation of Ethyl α-*s*-Butylacetonedicarboxylate

BY EVANS B. REID AND JOHN F. YOST

In connection with the synthesis of 3,5-di-*s*-butyl-*l*-cyclopentenealdehyde[1] various approaches were explored whereby it was hoped to synthesize α,α′-di-*s*-butylglutaric acid (auxin glutaric acid)[2] in quantities sufficient to permit the ultimate transformation of the latter into the appropriate ring system found in auxins a and b.[2] One of the most promising of these approaches appeared to be through the direct alkylation of ethyl acetonedicarboxylate by the Schroeter method.[3] The essential feature in this method is the slow addition of organic base (alkoxide) to a solution of the ester and two equivalents of alkyl halide. By this procedure Schroeter[3] was able to introduce two isopropyl groups into ethyl acetonedicarboxylate, though in poor yield. However there is no report of any attempt to alkylate this ester with the bulkier *s*-butyl group.

An attempted *dialkylation* using *s*-butyl iodide and sodium ethoxide according to Schroeter's directions resulted in the evolution of relatively large amounts of 2-butene. Moreover, when the product (which had been washed with an aqueous solution of sodium chloride) was vacuum distilled, considerable quantities of ethanol were eliminated. In spite of these undesirable by-products, however, a 14% yield of *mono-alkylated* ester was obtained. No evidence of di-alkylation could be found.

Experimentation showed that no 2-butane was evolved from a system containing ethanol, sodium ethoxide, ethyl acetonedicarboxylate and *s*-butyl iodide *provided* the temperature remained below 85° and the *p*H of the solution was not permitted to rise above 8.5. Increase of either temperature or *p*H above these values resulted in gas generation. Substitution of *s*-butyl bromide for the iodide required a higher reaction temperature and gave much 2-butene. It was also demonstrated that equally stringent conditions applied to the isolation of the alkylated ester. Traces of inorganic material, air, or nitrogen dried with calcium chloride rendered the vacuum distillation of the product erratic and resulted in the loss of ethanol.

Under optimum conditions a *mono-alkylation* experiment resulted in a 44% yield of ethyl α-*s*-butylacetonedicarboxylate, considerable tar and a crystalline substance which was identified as the tricarbethoxy resorcinol of Cornelius and von Pechmann[4] and Jerdan.[5] Formation of the latter compound is not encountered during dialkylations of this ester with primary alkyl halides, and its presence here in relatively large amounts is indicative of the inertia attendant upon alkylation with the *s*-butyl group.

When the mono-alkylated ester was treated again, under conditions of mild temperature and low *p*H, the product was a yellow slurry from which no pure compound could be isolated by distillation. A cursory study of this slurry indicated the presence of a mixture of salts. Likewise an attempted alkylation of the mono-alkylated ester under forcing conditions in benzene resulted in a complex mixture from which no dialkylated product could be obtained.

Finally it may be mentioned that attempted alkylation of ethyl 1,1,3,3-propanetetracarboxylate with *s*-butyl iodide was unsuccessful, as were attempts to couple diethyl *s*-butylmalonate with methylene iodide.

Acknowledgment.—Receipt of a grant-in-aid from the Hynson, Westcott and Dunning Fund is gratefully acknowledged.

Experimental

Ethyl α-*s*-Butylacetonedicarboxylate.—The optimum conditions for the alkylation consisted in adding a solution of 24 g. (1.05 moles) of sodium dissolved in 276 g. (6 moles) of absolute ethanol through a reflux condenser to a stirred solution of 202 g. (1.0 mole) of ethyl acetonedicarboxylate and 202 g. (1.10 moles) of *s*-butyl iodide in 100 g. of absolute ethanol. The rate of addition was such as to maintain the *p*H of the reactants at about 8.5. This required about 2.5 hours. The temperature of the reactants was maintained at about 80° during the addition of the base, and for an additional period of 6.5 hours. By this time the *p*H of the reactants was nearly 7, and only traces of 2-butene had formed (identified through its dibromide).[6] The alcohol was then removed under reduced pressure in a nitrogen atmosphere, and the residue was poured into ice-water. The ester layer was separated, and the aqueous layer was extracted with benzene. The combined ester and benzene extracts were washed with carbonate solution, dilute hydrochloric acid, and then several times with water. The wet benzene was removed by distillation under nitrogen at aspirator pressure, and the residue was distilled under nitrogen, at 0.10 mm., furnishing 114 g., or 44.2% of monoalkylated product, b.p. 108–110°. The product gave a positive enol (ferric chloride) test.

Anal. Calcd. for $C_{13}H_{22}O_6$: C, 60.4; H, 8.53. Found: C, 60.1; H, 8.48.

The residue from the vacuum distillation solidified to a yellow-brown slurry. The solid was obtained white by recrystallization from ethanol–water and from ligroin; m.p. 96.0–96.5°.

Anal. Calcd. for $C_{16}H_{20}O_8$: C, 56.6; H, 5.9. Found: C, 56.5; H, 6.0.

In all respects this enolic solid was similar to the compound $C_{16}H_{20}O_8$ obtained by Cornelius and von Pechmann[4] and by Jerdan[5] from the treatment of ethyl acetonedicarboxylate

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