[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Cleavage Reactions of Benzyl *n*-Propyl Ether with Boron Fluoride[1]

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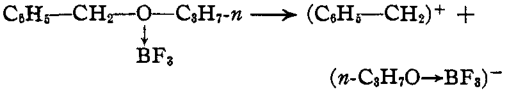
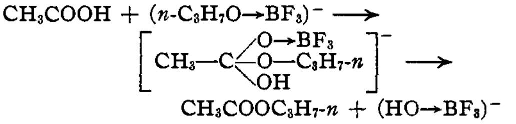
Introduction

The alkylations with alcohols, esters and ethers promoted by boron fluoride have been explained[2] on the assumption that the actual alkylating agent is an olefin obtained by the dehydration or cleavage of the alkylating reagent. Price and Ciskowski[3] opposed this view and preferred to explain these reactions by the positive fragment theory. In order to obtain further information with regard to such mechanisms benzyl *n*-propyl ether has been cleaved with boron fluoride, in the presence of other reagents. The reactions reported in this paper may be explained by assuming that the ether–boron fluoride complex reacts as an electrovalent compound, furnishing the positive benzyl fragment and the propoxyboron fluoride anion.



$$C_6H_5{-}CH_2{-}\underset{\underset{BF_3}{\downarrow}}{O}{-}C_3H_7\text{-}n \longrightarrow (C_6H_5{-}CH_2)^+ + (n\text{-}C_3H_7O{\rightarrow}BF_3)^- \quad (1)$$

In the presence of either acetic acid or acetic anhydride considerable *n*-propyl acetate was formed but no benzyl ester.



$$CH_3COOH + (n\text{-}C_3H_7O{\rightarrow}BF_3)^- \longrightarrow \left[CH_3{-}C\begin{matrix}\diagup O{\rightarrow}BF_3\\ {-}O{-}C_3H_7\text{-}n\\ \diagdown OH\end{matrix}\right]^- \longrightarrow CH_3COOC_3H_7\text{-}n + (HO{\rightarrow}BF_3)^- \quad (2)$$

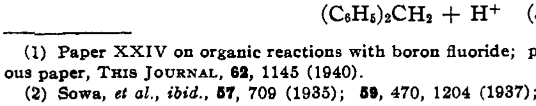
The positive benzyl fragment was transformed to viscous or solid polymer

$$x(C_6H_5CH_2)^+ \longrightarrow (C_7H_6)_x + H^+ \quad (3)$$

$$H^+ + (HO{\rightarrow}BF_3)^- \longrightarrow HOH{\cdot}BF_3 \quad (4)$$

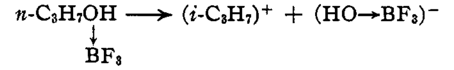
While no crystalline material could be extracted from these polymers, pyrolysis gave chiefly anthracene, indicative of the polybenzyl structure.

When the ether cleavage was conducted in the presence of aromatic compounds benzylbenzene, dibenzylbenzene, α-benzylnaphthalene and *p*-benzylphenol were obtained.



(5)

With 0.4 to 0.5 mole of boron fluoride per mole of ether the above reactions occurred exclusively. Presumably the propoxyl group was converted to *n*-propyl alcohol. The latter also could be consumed to some extent by doubling the amount of boron fluoride used. Some *iso*propylbenzene was obtained in this way. Isopropylation (without propylene) also may be explained by the positive fragment mechanism, assuming rearrangement to the iso form,[4] and further reaction as in (5).



$$n\text{-}C_3H_7\underset{\underset{BF_3}{\downarrow}}{O}H \longrightarrow (i\text{-}C_3H_7)^+ + (HO{\rightarrow}BF_3)^- \quad (6)$$

To show conclusively that the two ether groups react in different ways cleavage of benzyl *n*-propyl ether was accomplished in the presence of both acetic acid (or acetic anhydride) and benzene. *n*-Propyl acetate and benzylbenzene were obtained.

$$C_6H_5CH_2OC_3H_7\text{-}n + CH_3COOH + C_6H_6 \xrightarrow{BF_3} CH_3COOC_3H_7\text{-}n + (C_6H_5)_2CH_2 + H_2O \quad (7)$$

Breslow and Hauser[5] claim to have benzylated ethyl acetoacetate with benzyl chloride and boron fluoride to obtain ethyl α-benzylacetoacetate. Benzylation of ethyl acetoacetate with

TABLE I

CLEAVAGE REACTIONS OF BENZYL *n*-PROPYL ETHER[a]

Cleavage reagents	Moles	Boron fluoride, moles	Products and yields
Acetic acid	3	0.5	*n*-Propyl acetate, 58%; polymer, 70 g.
Acet. anhyd.	1.5	.5	*n*-Propyl acetate, 64%; polymer, 70 g.
Benzene	4	.54	Benzylbenzene, 33.3%; dibenzylbenzene, 22%
Benzene	3.3	1.0	Benzylbenzene, 46%; dibenzylbenzene, 28%; *iso*-propylbenzene, 10.5%
Naphthalene	2	0.53	α-Benzylnaphthalene, 48%.
Phenol	2.7	.5	*p*-Benzylphenol, 47.7%
Acetic acid Benzene	1.4 1.2	.45	*n*-Propyl acetate, 50%; benzylbenzene, 20.6%; dibenzylbenzene, 28.6%
Acet. anhyd. Benzene	2 4	.7	*n*-Propyl acetate, 64.7%; benzylbenzene, 48.3%; dibenzylbenzene, 23.2%

[a] One mole for each experiment.

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[1] Paper XXIV on organic reactions with boron fluoride; previous paper, THIS JOURNAL, **62**, 1145 (1940).

[2] Sowa, *et al.*, *ibid.*, **57**, 709 (1935); **59**, 470, 1204 (1937); **60**, 125, 654 (1938).

[3] Price and Ciskowski, *ibid.*, **60**, 2499 (1938).

[4] Whitmore, *ibid.*, **54**, 3274 (1932).

[5] Breslow and Hauser, *ibid.*, **62**, 2385 (1940).

benzyl *n*-propyl ether was attempted but the only products obtained were those which apparently were formed by ethyl acetoacetate condensation since the same material was obtained from ethyl acetoacetate and boron fluoride without benzyl *n*-propyl ether.

The experimental data are summarized in Table I.

Experimental

Preparation of Benzyl *n*-Propyl Ether.—Twelve hundred grams (20 moles) of *n*-propyl alcohol was placed in a three-liter, three-necked flask equipped with a mercury-sealed stirrer and reflux condenser. Ninety-two grams (4 moles) of sodium was added in small pieces. After the sodium was dissolved the reaction mixture was cooled in an ice-bath, care being taken that sufficient excess alcohol was present to prevent the sodium propylate from crystallizing. Then 506 g. (4 moles) of benzyl chloride was added with constant stirring over a period of thirty minutes. The mixture was stirred for an hour and then the temperature gradually raised to reflux. The excess alcohol was removed by distillation, 820 g. (14 moles) being recovered. Enough water was added to the reaction mixture (now a sludge) to dissolve the salt. Ether was added to take up the benzyl *n*-propyl ether and the two layers separated. The ether layer was washed with a small quantity of water and dried over calcium chloride. The benzyl *n*-propyl ether was distilled under vacuum and was obtained in 90–93% yields, based on the amount of benzyl chloride used: b. p. 68° at 8 mm., 96° at 24 mm.; $n^{20}\mathrm{D}$ 1.4905; d^{20} 0.9287.

Cleavage of Benzyl *n*-Propyl Ether with Acetic Acid.—Three moles (180 g.) of glacial acetic acid was placed in a weighed one-liter, three-necked flask equipped with mercury-sealed stirrer, reflux condenser and inlet tube. Boron fluoride was admitted, with cooling, until 0.4 to 0.5 mole was absorbed. One mole (150 g.) of benzyl *n*-propyl ether was then added slowly with constant stirring and cooling. The mixture was heated slowly over a water-bath and refluxed for two hours. Two layers separated. Ether and water were added and a curdy polymer (70 g.) separated which was removed and saved. The ether layer was washed with a small amount of water, neutralized with sodium carbonate solution, washed again with water and dried over calcium chloride. Distillation yielded *n*-propyl acetate, b. p. 99–101.5°, $n^{20}\mathrm{D}$ 1.3840. The yield was 59.3 g. or 58.1% based on the amount of benzyl *n*-propyl ether used.

The polymer recovered from the reaction mixture was pyrolyzed by atmospheric distillation. The product was redistilled and then purified by crystallizing twice from acetic acid. After sublimation the crystals melted at 201–204°. This compound was mixed with anthracene with melting point of 204–208°. The mixed melting point was 204–207°. The compound was oxidized with potassium dichromate and sulfuric acid in acetic acid. The oxidation product was crystallized from acetic acid and then from ethyl alcohol. The product melted at 273–280°. Mixed with anthraquinone (m. p. 280–283°) it melted at 278–283°. The oxidation product also gave a positive anthraquinone color test.[6]

Cleavage with Acetic Anhydride.—The procedure was the same as that described above. Instead of three moles of acetic acid, one and one-half moles of the anhydride was used with one mole of benzyl *n*-propyl ether. The same products were obtained: 65.6 g. of *n*-propyl acetate (64.3% yield), and 70 g. of polymer which yielded anthracene when treated as above.

Cleavage with Benzene.—A mixture of 312 g. (4 moles) of benzene and 150 g. (1 mole) of benzyl *n*-propyl ether was placed in a one-liter, three-necked flask equipped with mercury-sealed stirrer, reflux condenser, and inlet tube. The flask was immersed in an ice-bath and boron fluoride admitted until 37.0 g. (0.54 mole) was absorbed. The mixture was heated over a water-bath for two hours. This was followed by the addition of about 150 ml. of water. The benzene layer was separated, washed, neutralized with sodium carbonate, and dried over calcium chloride. The excess benzene was removed by distillation through a small packed column. The residue was distilled into rough fractions which upon redistillation yielded fractions boiling at 102–103° at 9 mm. and 185–195° at 5 mm. The first of these was identified as benzylbenzene, m. p. 25.5°, $n^{20}\mathrm{D}$ 1.5770, before freezing in the refractometer, and d^{20} 1.007. The compound was nitrated to give a product melting at 170° which checks with the 2,2′,4,4′-tetranitro derivative of benzylbenzene.[7] The yield was 56.0 g., or 33.3% based on the benzyl *n*-propyl ether. The second fraction was crystallized from alcohol and melted at 65–70°. This was recrystallized alternately from ethyl alcohol and ether according to the method described by Huston and Friedemann[8] to obtain pure *p*-dibenzylbenzene, m. p. 83–86°. From the combined filtrates a small amount of *o*-dibenzylbenzene melting at 77–78° was obtained. The total yield of dibenzylbenzenes was 28 g. or 21.8%.

Cleavage with Benzene and Excess Boron Fluoride.—The procedure was the same as in the preceding experiment except that 3.3 moles of benzene and 1 mole of boron fluoride were used. This experiment yielded 77.3 g. (46%) of benzylbenzene, 35.7 g. (27.7%) dibenzylbenzene, and a fraction boiling between 149 and 152° at atmospheric pressure. The 149–152° material had $n^{20}\mathrm{D}$ 1.4917 checking with $n^{20}\mathrm{D}$ 1.4922 for *i*-propylbenzene which boils at 152°. The yield of *i*-propylbenzene was 12.6 g. or 10.5%.

Cleavage with Naphthalene.—Boron fluoride (36 g., 0.53 mole) was added to a mixture of 260 g. (2 moles) of naphthalene and 150 g. (1 mole) of benzyl *n*-propyl ether contained in a one-liter, three-necked flask equipped with a mercury-sealed stirrer and reflux condenser. The reaction mixture was treated in the same manner as in the preceding experiments, ether being used to take up the products before the washing operations. The second distillation yielded two products, one boiling at 100–103° at 8 mm. and the other at 160–170° at 4 mm. The first fraction (151 g.) melted at 79.5° checking with 80.3° the melting point of naphthalene. The second fraction was crystallized from ethyl alcohol and melted at 57–58° in agreement with the melting point of α-benzylnaphthalene, 58°. The picrate melted correctly at 100°.[3] The yield of α-benzylnaphthalene was 105 g. or 48%.

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(6) Mulliken, "The Identification of Pure Organic Compounds," John Wiley and Sons, New York, N. Y., 1904, p. 216, Vol. I.

(7) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 1940, p. 218, second edition.

(8) Huston and Friedemann, THIS JOURNAL, 38, 2527 (1916).

Cleavage with Phenol.—The same procedure was followed as for naphthalene, using 257 g. (2.7 moles) of phenol, 150 g. (1 mole) of benzyl *n*-propyl ether and 34 g. (0.5 mole) of boron fluoride. Distillation gave 159 g. of unreacted phenol and a fraction which distilled at 161–165° at 5 mm. After crystallization from petroleum ether this product melted at 83–84°, checking the melting point of *p*-benzylphenol.[9] The yield was 87.7 g. (47.7%).

Cleavage with both Benzene and Acetic Acid.—To a solution of 95 g. of benzene (1.2 moles) and 80 g. of acetic acid (1.4 moles) was added 31 g. (0.45 mole) of boron fluoride. One mole (150 g.) of benzyl *n*-propyl ether was added slowly and the mixture refluxed for two hours before being washed and dried. Distillation yielded 51 g. (50%) of *n*-propyl acetate, 34.5 g. (20.6%) of benzylbenzene, and 37 g. (28.6%) of dibenzylbenzene. These products were identified as in the preceding experiments.

Cleavage with both Benzene and Acetic Anhydride.—The procedure was the same as in the preceding experiment. The amounts of reagents were as follows: 312 g. (4 moles) of benzene, 204 g. (2 moles) of acetic anhydride, 48 g. (0.7 mole) of boron fluoride, and 150 g. (1 mole) of benzyl *n*-propyl ether. Yields were 66 g. (64.7%) of *n*-propyl acetate, 81 g. (48.3%) of benzylbenzene, and 30 g. (23.2%) of dibenzylbenzene.

Reaction with Ethyl Acetoacetate.—Boron fluoride was passed into a solution of 262 g. (2 moles) of ethyl acetoacetate and 150 g. (1 mole) of benzyl *n*-propyl ether until 32.3 g. (0.48 mole) was absorbed. After treatment as above distillation yielded 147 g. distilling at 48–60° at 5–8 mm., $n^{20}\text{D}$ 1.4398 to 1.4845 (identified as a mixture of unreacted ethyl acetoacetate and benzyl *n*-propyl ether); 22.2 g. at 125–135° at 3 mm., $n^{20}\text{D}$ 1.4998 to 1.5178 (which yielded, from ammonium hydroxide in acetone solution, leaflet crystals[10] melting at 97–100°); 19.3 g. at 140–160° at 3 mm., $n^{20}\text{D}$ 1.5248 to 1.5291 (which gave no solid derivative with ammonium hydroxide in acetone or with ammonia). When the experiment was repeated without the benzyl *n*-propyl ether fractions were obtained distilling at 123–130° at 3 mm., $n^{20}\text{D}$ 1.5040 to 1.5135 (which yielded, from ammonium hydroxide in acetone solution, leaflet crystals melting at 97–99°); and at 140–170° at 3 mm., $n^{20}\text{D}$ 1.5085 (which gave no solid product with ammonium hydroxide in acetone solution or with liquid ammonia).

Summary

The alkylation of acetic acid, acetic anhydride, benzene, naphthalene and phenol with benzyl *n*-propyl ether in the presence of boron fluoride has been studied. Ethyl acetoacetate did not alkylate under the conditions employed.

A mechanism for the alkylation reactions has been suggested based on the cleavage of the benzyl *n*-propyl ether into a positive benzyl fragment and a negative *n*-propoxyl ion.

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[9] Zincke and Walter, *Ann.*, **334**, 367 (1904).

[10] Ethyl α-benzylacetoacetate boils at 155–167° at 12 mm. and yields an amide, m. p. 149–150° (ref. 5).

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[Contribution from the National Institute of Health, U. S. Public Health Service]

Synthesis of the Epimer of Cellobiose (4-[β-D-Glucopyranosido]-D-mannose)[1]

By W. T. Haskins, Raymond M. Hann and C. S. Hudson

Attention was recently[2] directed to the possibility of using 2,3-isopropylidene-D-mannosan-<1,5>β<1,6> (or, in short, acetone-D-mannosan) for the synthesis of disaccharides which are linked through carbon atom four of D-mannose. The present article describes the synthesis of the epimer of cellobiose, namely, 4-[β-D-glucopyranosido]-D-mannose, the disaccharide which was first prepared synthetically from cellobiose through cellobial by Bergmann and Schotte.[3] Acetobromo-D-glucose, by slight modification of the conditions for disaccharide synthesis described by Reynolds and Evans, condenses with acetone-D-mannosan to form in about 25 to 30% yield the crystalline 2,3-isopropylidene-4-[2,3,4,6-tetraacetyl-β-D-glucosido]-D-mannosan<1,5>β<1,6> (I), which upon treatment with boiling 80% acetic acid loses the isopropylidene residue and forms 4-[2,3,4,6-β-tetraacetyl-D-glucosido]-D-mannosan (II). The latter compound readily acetylates by usual methods to form 2,3-diacetyl-4-[2,3,4,6-tetraacetyl-β-D-glucosido]-D-mannosan<1,5>β<1,6> (III). The 1,6-mannosan ring of this anhydro disaccharide is readily ruptured, with concurrent acetylation on carbon atoms one and six, upon treating the compound with an acid acetylating mixture, the product being the well known α-octaacetate of 4-β-D-glucopyranosido-D-mannose (IV). The octaacetate upon deacetylation with barium methylate yields the parent disaccharide, 4-β-D-glucopyranosido-D-mannose, in the form of the known well characterized monohydrate of the alpha form.

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[1] Publication authorized by the Surgeon General, U. S. Public Health Service. (Not copyrighted.)

[2] Knauf, Hann and Hudson, This Journal, **63**, 1447 (1941).

[3] Bergmann and Schotte, *Ber.*, **54**, 1564 (1921).