[DEPARTMENT OF CHEMISTRY AND PURDUE RESEARCH FOUNDATION, PURDUE UNIVERSITY]

The Reaction of Benzyl Halides with the Sodium Salt of 2-Nitropropane.[1] A General Synthesis of Substituted Benzaldehydes

BY H. B. HASS AND MYRON L. BENDER[2]

Alkylation of nitro paraffin salts, as described in the literature,[3,4,5,6,7,8] may occur as carbon-alkylation, forming a new carbon–carbon bond, or oxygen-alkylation, leading to an instable nitronic ester which breaks down into an oxime and a carbonyl compound. *p*-Nitrobenzyl chloride,[7,8] *o*-nitrobenzyl chloride,[3] and 2,4-dinitrobenzyl chloride[7] are the only benzyl halides reported to give carbon-alkylation with simple nitroparaffin salts.[9] Other halides such as benzyl chloride and *p*-cyanobenzyl chloride have been reported to give oxygen-alkylation with nitro paraffin salts.[7] Data in the literature[4,5] on the reaction between nitro paraffin salts and halides other than benzyl halides indicate predominantly oxygen-alkylation.

Since the above data were collected by various workers utilizing varied procedures, it was decided to investigate the alkylation reaction in the benzyl halide series utilizing a uniform procedure. 2-Nitropropane was chosen as the nitro paraffin in the following investigations because it is readily available and because primary nitro paraffins give two products (monoalkylated and dialkylated) which complicate the interpretation of results. The sodium salt of the nitro paraffin has been used because of its ease of preparation. Ethanol has been the usual alkylation solvent because it is an effective solvent for both nitro paraffin salt and alkyl halide, and because it is easily separable from the products of the reaction. In studying the alkylation reaction, three new para-substituted benzyl halides were prepared: *p*-acetobenzyl bromide, *p*-trifluoromethylbenzyl bromide, and (*p*-iodomethylphenyl)-trimethylammonium iodide.

Each of nine substituted benzyl halides was treated with sodium 2-propanenitronate[10] in ethanol. In every case except *p*-nitrobenzyl chloride the corresponding substituted benzaldehyde was obtained in 68–77% yield. An example is given in Fig. 1. *p*-Nitrobenzyl chloride gave only 1% of *p*-nitrobenzaldehyde but gave an 83% yield of 2-methyl-2-nitro-1-(*p*-nitrophenyl)-propane as shown in Fig. 2.

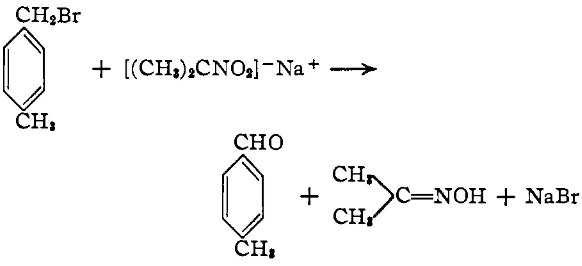

Fig. 1.

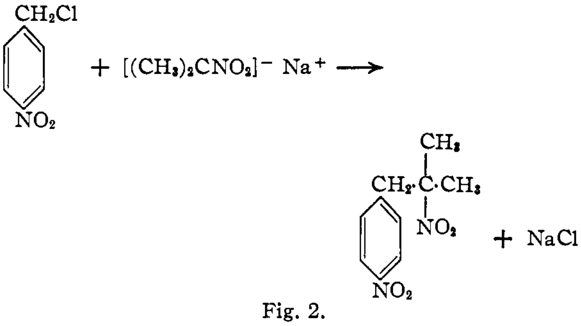

Fig. 2.

The results of the alkylation reaction of nine substituted benzyl halides are summarized in Table I. These data indicate that the reaction described is not productive of carbon-alkylation except in the isolated case of *p*-nitrobenzyl chloride, but that the method described is a general one for the preparation of para-substituted benzaldehydes with the lone exception of *p*-nitrobenzaldehyde. This synthesis, in general, is comparable to the Sommelet reaction[11]; however, the former gives slightly higher yields in some cases. Like the Sommelet reaction, this synthesis has several advantages. First, substituted benzaldehydes can be produced by simple synthetic means such as halogenation, hydrohalogenation or halomethylation of the proper compound followed by treatment with sodium 2-propanenitronate. Second, substances sensitive to oxidation can be converted in this manner to carbonyl compounds without recourse to oxidative conditions.

The experimental procedure for only one alkylation, the alkylation of sodium 2-propanenitronate with *p*-xylyl bromide is described in the experimental section. It is, however, representative of the simple method used in all the alkylation reactions.

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(1) An abstract of a thesis by Myron L. Bender, submitted to the Faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1948. Presented before the Division of Organic Chemistry, 114th American Chemical Society meeting, St. Louis, Missouri, September 6, 1948.

(2) J. K. Lilly Fellow, 1947; American Cyanamid Company Fellow, 1947–1948; present address: Harvard University, Cambridge 38, Massachusetts.

(3) Posner, *Ber.*, **31**, 657 (1898).

(4) Nenitzescu and Isacescu, *ibid.*, **63**, 2484 (1930).

(5) Hantzsch, *Z. anorg. allgem. Chem.*, **209**, 213 (1932).

(6) Thurston and Shriner, *J. Org. Chem.*, **2**, 183, 560 (1937–1938).

(7) Weisler and Helmkamp, THIS JOURNAL, **67**, 1167 (1945).

(8) Hass, Berry and Bender, *ibid.*, **71**, in press (1949).

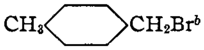
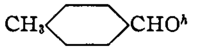
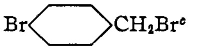
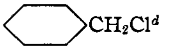
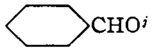
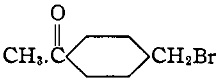
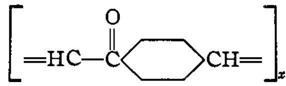
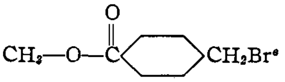
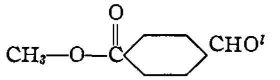
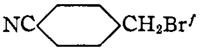
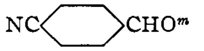
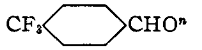
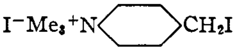
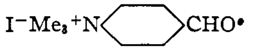
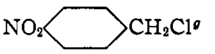
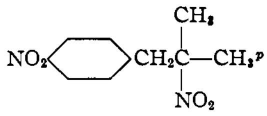
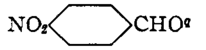
(9) Rich, Rose and Wilson, *J. Chem. Soc.*, 1234 (1947), report carbon-alkylation with the silver salt of nitroform and bis- and tris-iodomethylbenzenes.

(10) Sodium 2-propanenitronate is used to designate the sodium salt of 2-nitropropane, the pseudo acid which is a tautomer of 2-propanenitronic acid. This follows accepted nomenclature for carboxylic, sulfonic, phosphonic and many other organic acids.

(11) Sommelet, *Compt. rend.*, **157**, 852 (1913).

Table I

Reaction of Para-substituted Benzyl Halides and Sodium 2-Propanenitronate[a]

Halide	Time, hours	Temp., °C.	Carbon alkylation	Oxygen alkylation	Product	Yield, %	B. p. or m. p., °C.	n^{20}_D
	15	25		X		70	68-72 (6 mm.)	1.5420
	15	25		X		75	56-57	
	3	80		X		73	63-64 (13 mm.)	1.5446
	15	25		X		77	Softens at 300	
	1	80		X		72	61-63	
	5	80		X		70	95-96	
	2	25		X		77	66-67 (13 mm.)	1.4630
	0.33	80		X		68	152 dec.	
	1	80	X	X		83	64-66	
						1	104-106	

[a] In addition to benzaldehydes, ketones with both aromatic and aliphatic sustituents have been prepared. 2-Octanone has been prepared from 2-bromoöctane in 54% yield according to the general procedure described. Preliminary attempts to prepare aliphatic aldehydes have failed, however, apparently because the basic reaction conditions catalyzed the condensation of the aldehyde formed. Further examples of the synthesis of ortho-, meta- and para-substituted benzaldehydes and the synthesis of ketones by this general procedure will be described in a subsequent paper. [b] M.p. 34-35°. [c] M. p. 61-63°. [d] n^{20}_D 1.5395. [e] M. p. 53-55°. [f] M. p. 113-115°. [g] M. p. 70-71°. [h] Semicarbazone, m. p. 232-234°. [i] Semicarbazone, m. p. 228-229°. [j] 2,4-Dinitrophenylhydrazone, m. p. 234-235°. [k] This polymer was apparently formed by the aldol condensation of *p*-acetobenzaldehyde followed by dehydration. See Russell, This Journal, **70**, 2864 (1948), for a similar polymerization. *Anal.* Calcd. for $(C_9H_6O)_x$: C, 83.05; H, 4.65. Found: C, 83.0; H, 4.72. [l] Phenylhydrazone, m. p. 142-144°. [m] Phenylhydrazone, m. p. 144-145°. [n] *Anal.* Calcd. for $C_8H_5F_3O$: C, 55.18; H, 2.87; F, 32.73. Found: C, 55.0; H, 3.26; F, 31.0. [o] *Anal.* Calcd. for $C_{10}H_{14}INO$: C, 41.25; H, 4.84; N, 4.83. Found: C, 41.5; H, 4.76; N, 4.90. [p] Lit. m. p. 65-66°.[8] [q] Semicarbazone, m. p. 220°.

Experimental[12]

p-Acetobenzyl Bromide

(a) **p-Cyanobenzyl Methyl Ether.**—A solution of sodium (18.4 g., 0.80 mole) in 125 ml. of methanol was added dropwise to a benzene solution of *p*-cyanobenzyl bromide (141 g., 0.73 mole). The mixture was refluxed for one hour, cooled, and filtered; the filtrate was washed with water, dried, and distilled. An 84% yield of *p*-cyanobenzyl methyl ether was obtained; 89 g.; b. p. 101-102° (4 mm.); n^{20}_D 1.5266.

Anal. Calcd. for C_9H_9NO: C, 73.44; H, 6.16. Found: C, 73.2; H, 6.1.

(b) **p-Acetobenzyl Methyl Ether.**—Methylmagnesium iodide prepared from magnesium turnings (6.50 g., 0.242 mole) and methyl iodide (34.4 g., 0.242 mole) was treated with *p*-cyanobenzyl methyl ether (29.7 g., 0.20 mole). The mixture was refluxed for five hours and then poured into a cold aqueous solution of ammonium chloride. The organic layer was washed with water, dried, and distilled. Twenty grams of *p*-acetobenzyl methyl ether was obtained; yield 62%; b. p. 107-109° (3.5 mm.); n^{20}_D 1.5287.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.38. Found: C, 73.4; H, 7.18.

(c) **p-Acetobenzyl Bromide.**—*p*-Acetobenzyl methyl ether (10 g., 0.061 mole) was treated with 48% hydrobromic acid (30 g., 0.18 mole). Six grams of *p*-acetobenzyl bromide was obtained; yield 46%; b. p. 134-136° (5 mm.); m. p. 32-33°.

Anal. Calcd. for C_7H_9BrO: C, 50.83; H, 4.25; Br, 37.51. Found: C, 51.3; H, 4.19; Br, 37.1.

p-Trifluoromethylbenzyl Bromide

(a) **Ethyl p-Trifluoromethylbenzoate.**—Absolute ethanol (92 g., 2.0 moles) was added dropwise to *p*-trifluoromethylbenzoyl chloride (125 g., 0.60 mole) at 15° using pyridine as catalyst. The solution was refluxed for three hours and distilled. An 85% yield of ethyl *p*-trifluoromethylbenzoate was obtained; 110 g., b. p. 80.0-80.5° (5.5 mm.); n^{20}_D 1.4478; lit. b. p. 80-81 (5 mm.); n^{20}_D 1.448.[13]

(b) **p-Trifluoromethylbenzyl Alcohol.**—Ethyl *p*-trifluoromethylbenzoate (44 g., 0.20 mole) was treated with lithium aluminum hydride (5.72 g., 0.15 mole) according to the method of Nystrom and Brown.[14] Thirty-three grams of *p*-trifluoromethylbenzyl alcohol was obtained; yield 94%; b. p. 78.5-80° (4 mm.); n^{20}_D 1.4600.

Anal. Calcd. for $C_8H_7F_3O$: C, 54.56; H, 3.98; F, 32.35. Found: C, 54.3; H, 4.26; F, 32.1.

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[12] All melting points are corrected. Microanalyses by Mr. A. Coleman, Mr. H. Galbraith and Miss L. Roth.

[13] McBee and Graham, unpublished results.

[14] Nystrom and Brown, This Journal, **69**, 1197 (1947).

(c) *p*-Trifluoromethylbenzyl Bromide.—*p*-Trifluoromethylbenzyl alcohol (35 g., 0.20 mole) was treated with 48% hydrobromic acid (105 g., 0.65 mole). A 90% yield of *p*-trifluoromethylbenzyl bromide was obtained; b. p. 65-66° (5 mm.); n^{20}D 1.4918.

Anal. Calcd. for $C_8H_6F_3Br$: C, 40.00; H, 2.51; Br, 33.43. Found: C, 40.2; H, 2.74; Br, 33.7.

(*p*-Iodomethylphenyl)-trimethylammonium Iodide

(a) *p*-Dimethylaminobenzyl Alcohol.—This procedure is far superior to that reported in the literature.[15] *p*-Dimethylaminobenzaldehyde (50 g., 0.33 mole) was treated with lithium aluminum hydride (4.2 g., 0.11 mole) according to the method of Nystrom and Brown.[14] A 75% yield of *p*-dimethylaminobenzyl alcohol was obtained; 38 g.; b. p. 116.5-117° (1 mm.); n^{20}D 1.5795; lit. b. p. 123° (1 mm.); n^{20}D 1.5701.[15]

(b) (*p*-Hydroxymethylphenyl)-trimethylammonium Iodide.—*p*-Dimethylaminobenzyl alcohol was treated with methyl iodide in acetone according to the method of Smith and Welch[15]; m. p. 231-232° dec.; lit. m. p. 232° dec.[15].

(c) (*p*-Iodomethylphenyl)-trimethylammonium Iodide.—(*p*-Hydroxymethylphenyl)-trimethylammonium iodide (19.5 g., 0.066 mole) was mixed with 57% hydriodic acid (75 ml., 127 g., 0.57 mole) with occasional shaking for two days at 25°. The fine needles which crystallized were filtered, washed with acetone, and dried. Twenty-one grams of product was collected; yield 79%; m. p., after recrystallization, 200-250° dec.

Anal. Calcd. for $C_{10}H_{15}I_2N$: C, 29.80; H, 3.75; N, 3.48. Found: C, 29.7; H, 3.72; N, 3.51.

Reaction of Sodium 2-Propanenitronate and *p*-Xylyl Bromide.—Sodium (1.15 g., 0.05 mole) was dissolved in 50 ml. of absolute ethanol. 2-Nitropropane (5.8 g., 0.065 mole) and then *p*-xylyl bromide (9.3 g., 0.05 mole) were added. The mixture was left at room temperature for fifteen hours. The precipitated sodium bromide was filtered and the filtrate was concentrated at atmospheric pressure to remove the ethanol. The resulting mixture was dissolved in ether and water. The ethereal solution was washed with 10% sodium hydroxide solution to remove acetoxime[16] and excess 2-nitropropane, washed with water and then dried with sodium sulfate. The ether was evaporated and the *p*-tolualdehyde was distilled; yield 4.2 g., 70%; b. p. 68-72° (6 mm.); n^{20}D 1.5420.

Summary

A general procedure for the conversion of para-substituted benzyl halides to the corresponding para-substituted benzaldehydes is described. This is effected through the reaction of the halide with sodium 2-propanenitronate. The benzaldehydes are generally obtained in 68–77% yield. *p*-Nitrobenzyl chloride, alone, fails to give the corresponding benzaldehyde in good yield; it is converted mainly to 2-methyl-2-nitro-1-(*p*-nitrophenyl)-propane.

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[15] Smith and Welch, *J. Chem. Soc.*, 730 (1934).

[16] In one exploratory experiment acetoxime was isolated at this point by repeated water extraction followed by continuous extraction of the aqueous solution with ether.

LAFAYETTE, INDIANA RECEIVED JULY 26, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of the Sulfation of Optically Active Secondary Butyl Alcohol

BY ROBERT L. BURWELL, JR.

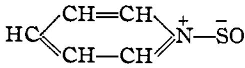
Sulfuric acid, the dioxane sulfur trioxide addition compound, and chlorosulfonic acid react with (+)*s*-butyl alcohol to give (+)barium *s*-butyl sulfate.[1] If, as would appear likely, at least one of these reagents acts without affecting the carbon-oxygen bond of the alcohol, the (+)alcohol is configurationally related to the (+)salt. Since treatment of salt, prepared by action of the dioxane sulfur trioxide complex, with solutions of alkali regenerates an alcohol of opposite but nearly equal rotation, the reaction with dioxane sulfur trioxide proceeds nearly without loss of optical purity.[2] Correspondingly, the configurations in the particular preparations with sulfuric and with chlorosulfonic acids were +22% and +12%.[3]

Other methods of preparing *s*-butyl sulfates have now been investigated. Since barium *s*-butyl sulfate apparently decomposes at room temperatures, the sodium salt has been used as the reference material.

The pyridine sulfur trioxide complex reacts with optically active *s*-butyl alcohol to give a product whose configuration is substantially + 100%.

While sulfamic acid reacts with primary alcohols to give ammonium alkyl sulfates, it has been reported not to react with secondary alcohols.[4] Actually, however, small yields result from heating *s*-butyl alcohol and sulfamic acid at 100° but the reaction, at any rate, is difficult. The addition of pyridine greatly facilitates the reaction and permits good yields to be obtained. The configuration of the product is substantially + 100%. This is a most convenient way of making the alkali metal *s*-butyl sulfates and presumably those of many other secondary alcohols since sulfamic acid is much easier to handle than sulfur trioxide or chlorosulfonic acid. The sulfamic acid pyridine reagent has been used to sulfate the phenolic hydroxyls of stilbesterol.[5]

Baumgarten[6] has argued plausibly that sulfamic acid is best represented as an inner salt, $H_3\overset{+}{N}—\overset{-}{S}O_3$, analogous to the pyridine sulfur trioxide addition compound



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[1] Burwell, THIS JOURNAL, **67**, 220 (1945).

[2] Burwell and Holmquist, *ibid.*, **70**, 878 (1948).

[3] The + indicates that the reaction proceeds with retention of configuration; the number indicates the per cent. of maximum rotation relative to the starting compound.

[4] Cupery, *Ind. Eng. Chem.*, **30**, 627 (1938).

[5] Short and Oxley, British Patent 577,666, May 27, 1946; *C. A.*, **41**, 2084 (1947).

[6] Baumgarten, *Ber.*, **62**, 820 (1929).