[CONTRIBUTION OF THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Isomerization during the Preparation of *n*-Amyl Chloride

BY FRANK C. WHITMORE, F. A. KARNATZ AND A. H. POPKIN

Recent studies[1,2] have been made on the formation of isomeric chlorides by the action of zinc chloride and hydrochloric acid on methylneopentylcarbinol and on 2-ethyl-1-butanol. Formation of the equilibrium mixture of 2- and 3-chloropentane on treatment of either with zinc chloride and hydrochloric acid also has been reported.[3]

To determine whether isomerization could occur through the halide, *n*-amyl chloride prepared in 80% yields by the action of thionyl chloride on *n*-amyl alcohol in pyridine was treated with the same reagents. Only 3% of a mixture of 2- and 3-chloropentanes was isolated. The formation of more rearranged products during the replacement of hydroxyl by halogen than by similar treatment of the pure halide with zinc chloride and hydrochloric acid is significant.

The *n*-amyl chloride obtained from thionyl chloride was free from traces of isomerized chlorides, which is in agreement with previously recorded results.[4] The index of refraction n^{20}D 1.4128 was higher than the values of n^{20}D 1.41192[5] and 1.4120[6] in the literature. The *n*-amyl chloride recovered from the action of zinc chloride and hydrochloric acid on the pure *n*-amyl chloride had n^{20}D 1.4120. Moreover, the *n*-amyl chloride obtained from the treatment of *n*-amyl alcohol with zinc chloride and hydrochloric acid had a refractive index range of n^{20}D 1.4119–1.4121 which was raised to n^{20}D 1.4128 only after two refractionations through a 12-plate column.[7] It is apparent that the low refractive index values previously recorded for *n*-amyl chloride were due to traces of 2- and 3-chloropentanes.

The synthesis of *n*-amyl alcohol involved the preparation of a large quantity of *n*-butyl bromide by the action of sulfuric acid and hydrobromic acid on *n*-butyl alcohol. A careful investigation of the low boiling by-products gave no indication of the formation of rearranged products in this reaction.

Experimental

Action of Sulfuric Acid and Hydrobromic Acid on *n*-Butyl Alcohol.—*n*-Butyl bromide was prepared by the action of sulfuric acid and hydrobromic acid[8] on 12 moles of a very pure sample of *n*-butyl alcohol.[9] The product was fractionated at 731 mm. to give: fraction 1, 1.4 g., 93°, n^{20}D 1.4203; 2, 35.3, 96°, 1.4387; 3, 34.3, 98°, 1.4389; 4–5, 72.8, 99°, 1.4390; 6–15, 1270, 99–99.5° (734 mm.), 1.4390–1.4392.

To determine whether *s*-butyl bromide was present as rearranged product, fractions 1–5 were refractionated to give: 16, 7.7 g., 75–98° (734 mm.), n^{20}D 1.4352; 17, 10.7, 98°, 1.4389; 18–19, 113.8, 99.4–100.0°, 1.4392. Fraction 16 was then refractionated to give: 20, 0.56 g., n^{20}D 1.4102; 21, 0.9, 1.4366; 22, 0.4, 1.4385. The fractionation was conducted at a vapor velocity too low for significant temperature reading but the refractive index of fraction 20 indicates the depression in the indices to be due to a small amount of olefin with no indication of the presence of *s*-butyl bromide.

Preparation of *n*-Amyl Alcohol.—*n*-Butylmagnesium bromide was prepared by the addition of 685 g. (5 moles) of *n*-butyl bromide to 122 g. of magnesium in 1500 cc. of ether. The Grignard reagent was cooled to salt-ice temperature, a liter of ether added and formaldehyde, generated from paraformaldehyde at 175° and passed through a heated tube, was added until no further test for Grignard reagent was obtained. The complex was decomposed on ice and the product steam distilled. The resulting oil layer was washed with sodium bisulfite solution and dried over anhydrous potassium carbonate. Fractionation at 733 mm. gave: fractions 1–3, 19 g., 129–134°, n^{20}D 1.3972–1.4081; 4–22, 274 g., 136°, 1.4093; residue 11 g., yield 68%. A similar run was completed and all fractions of constant boiling point and constant refractive index were combined and refractionated at 100 mm. to give a forerun of two fractions, 15 g., 86°, n^{20}D 1.4080–1.4097; twenty-eight fractions, 87°, 1.4093, and weight 396 g. The constants for pure *n*-amyl alcohol were: 136.8° (734 mm.), 137.8° (760 mm.), using a Cottrell apparatus;[10] n^{20}D. 1.40988 ± 0.00005;[11] freezing point, $-78.24°$, and d^{20}_4 0.8144.

Action of Zinc Chloride and Hydrochloric Acid on *n*-Amyl Alcohol.—A solution of 819 g. (6 moles) of fused zinc

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(1) Whitmore and James, unpublished work.

(2) Whitmore and Karnatz, THIS JOURNAL, **60**, 2533 (1938).

(3) This suggested the possibility of obtaining 2- and 3-chloropentane as by-products in the preparation of *n*-amyl chloride from the alcohol, zinc chloride and hydrochloric acid. Synthetic *n*-amyl alcohol was treated with zinc chloride and hydrochloric acid to give a 57% yield of *n*-amyl chloride. A 10% yield of a mixture of 2- and 3-chloropentanes was isolated from the low boiling products.

(4) McKenzie and Clough, *J. Chem. Soc.*, **103**, 687 (1913); Kirner, THIS JOURNAL, **50**, 1958 (1928); Gilman and Harris, *Rec. trav. chim.*, **50**, 1052 (1931).

(5) Karvonen, *Ann. Acad. Sci. Fenn.*, **A5**, No. 6, 124 (1914); *Chem. Abst.*, **14**, 2176 (1920).

(6) Rank, *J. Chem. Phys.*, **1**, 572–575 (1933).

(7) Whitmore and Lux, THIS JOURNAL, **54**, 3448 (1932); Wilson, Parker and Laughlin, *ibid.*, **55**, 2795 (1933).

(8) *Org. Syntheses*, **1**, 5 (1921).

(9) THIS JOURNAL, **54**, 3443 (1932).

(10) Quiggle, Tongberg and Fenske, *Ind. Eng. Chem.*, *Anal. Ed.*, **6**, 466 (1934).

(11) Abbe type, Valentine refractometer checked by Bureau of Standards.

chloride in 606 g. of concentrated aqueous hydrochloric acid was heated for twelve hours at 113–128° with 264 g. (3 moles) of *n*-amyl alcohol. Stirring was conducted rapidly during reaction with vigorous refluxing. The amyl chloride layer was separated, washed with distilled water and a 10% solution of potassium carbonate. The chloride was then dried and fractionated at 736 mm. to give: 1, 2.0 g., 37–91°, n^{20}_{D} 1.3894; 2, 19, 91–99°, 1.4092; 3, 22, 100–104°, 1.4112; 4, 22.2, 104–105°, 1.4117; 5–10, 105–106.5° (739 mm.), 183.1 g., 1.4119–1.4122. The 183.1 g. (57% yield) of fractions 5–10 was *n*-amyl chloride.

Fractions 2, 3 and 4 were refractionated at 733 mm. to give: 11, 1.2 g., 71–92.2°, n^{20}_{D} 1.4032; 12, 9.8, 93.2°, 1.4082; 13, 13.2 g., n^{20}_{D} 1.4092; 14, 11.5, 1.4112; 15, 7.4, 1.4122. Fractions 12, 13 and 14 were again refractionated at 735 mm. to give: 16, 1.5 g., 90–95°, n^{20}_{D} 1.4071; 17, 11.2, 95°, 1.4084; 18, 11.7, 96°, 1.4092; 19, 2.8, 96–102°, 1.4110; 20, 4.1, n^{20}_{D} 1.4120; residue, 1.5 g. Fraction 2 was converted to the Grignard reagent, treated with phenyl isocyanate and the complex decomposed with ice and hydrochloric acid. The ether layer, after many recrystallizations from ethyl alcohol, gave methyl-*n*-propylacetanilide, m. p. and mixed m. p. 95–96°, proving the presence of 2-chloropentane. Fractional crystallization of the crystals from the mother liquor yielded a product, m. p. 121–122.5°, which when mixed with known diethylacetanilide, m. p. 127–128°, gave a mixed m. p. of 122–125°. This indicated the presence of 3-chloropentane.

To verify the mixed melting point for diethylacetanilide, the following microscopic analysis was made.[12] The known diethylacetanilide, melting at 127–128°, crystallized in needles from ethyl alcohol (system probably triclinic), gave negative elongation and the following refractive indices (approximate, white light): η_α 1.516–1.519, η_β 1.535–1.540, η_γ 1.627–1.628; sign +, 2V = 32° and extinction angle 26°. The crystal analysis for the diethylacetanilide obtained from the rearranged 3-chloropentane, 121–122.5°, was identical with that of the known, above. Crystal analysis for methyl-*n*-propylacetanilide yielded: $\eta_\alpha > 1.520$, η_γ 1.625–1.630 for white light; sign +, negative elongation and parallel extinction.

Preparation of Pure *n*-Amyl Chloride.—*n*-Amyl chloride free from 2- and 3-chloropentanes was prepared by treating commercial (Sharples) *n*-amyl alcohol in pyridine with thionyl chloride.[13] A solution of 440 g. (5 moles) of fractionated commercial *n*-amyl alcohol, 136° (732 mm.), n^{20}_{D} 1.4107–1.4109, in 435 g. (5.5 moles) of fractionated commercial pyridine, 113.0° (735 mm.), n^{20}_{D} 1.5097, was treated with 772.5 g. (6.5 moles) of thionyl chloride at −10°. The reaction mixture was warmed to 104° during six hours and that temperature maintained for one and one-half hours. Sulfur dioxide was liberated at 73–104°. Three similar preparations of varying quantities of reactants failed to yield a sharp decomposition temperature for the alcohol–thionyl chloride complex. Decrease in the rate of thionyl chloride addition to one and three-fourths hours per mole and increase in length of heating period to five hours per mole did not improve the yield of chloride.

The crude chloride was separated in the usual way and fractionated to give at 741 mm.: fractions 1–3, 24.2 g., 106–106.5°, n^{20}_{D} 1.4122–1.4123; 4–14, 394.7, 106.5°, 1.4126–1.4128; 15, 5.1, 106.5°, 1.4130; residue 56 g. The total halide formed, 424 g., was *n*-amyl chloride in 80% yield. The three additional preparations using thionyl chloride also gave *n*-amyl chloride, n^{20}_{D} 1.4126–1.4128. The constants for refractionated *n*-amyl chloride were: b. p. 106° (725 mm.), n^{20}_{D} 1.41280 ± 0.00005, d^{20}_4 0.8828; *MR*, calcd., 30.15; obsd., 30.08.

Reaction of *n*-Amyl Chloride with Zinc Chloride and Hydrochloric Acid.—All fractions of *n*-amyl chloride having values of n^{20}_{D} 1.4126–1.4128 were combined and refractionated through column A to give at 741 mm.: 1, 0.5 g., 91°, n^{20}_{D} 1.4134; 2–3, 5.9, 96°, 1.4127; 4, 1.2, 102°, 1.4127; 5–19, 503.4, 106°, 1.4127; 20–25, 229.3, 106°, 1.4128. Into a two-necked two-liter round-bottomed flask was placed a solution of 819 g. (6 moles) of zinc chloride in 606 g. of concentrated aqueous hydrochloric acid. To this was added rapidly 319.5 g. (3 moles) of *n*-amyl chloride of fractions 7–11 and 13–17, above. The temperature of the bath was kept at 126–134° for twelve hours with vigorous stirring and rapid refluxing. The resulting chloride layer was separated, washed with distilled water, and a 10% solution of sodium carbonate. The chloride was dried and fractionated at 740 mm. to give: 1, 0.5 g., 32–50°, n^{20}_{D} 1.3837; 2, 3.9, 50–96°, 1.4085; 3, 9.0, 96–103°, 1.4108; 4, 6.5, 103–105°, 1.4108; 5–6, 16.4, 105°, 1.4109; 7–11, 39.8, 105.2°, 1.4110–1.4114; 12–22, 194.9, 104.5–105.5° (732 mm.), 1.4118–1.4120; residue, 3.5 g.; 14 g. of olefin was collected in a dry ice–acetone trap.

Fractions 2–11 were combined and fractionated at 741 mm. to give: 23, 1.5 g., 56–90°, n^{20}_{D} 1.4012; 24, 4.6, 1.4086; 25, 4.3, 101–103°, 1.4100; 26, 3.6, 104–105°, 1.4106; 27, 4.4, 105°, 1.4110; 28, 105–106°, 14.2, 1.4119. The remainder was *n*-amyl chloride. Based on fractions 24, 25 and part of 26, the yield of rearranged product is 3%. Fraction 24 was converted to the Grignard reagent, treated with phenyl isocyanate, and worked up in the usual manner. After many crystallizations from ethyl alcohol, methyl-*n*-propylacetanilide was obtained, m. p. and mixed m. p. 95–96°, proving the presence of 2-chloropentane. 3-Chloropentane was also probably present as an isomerization product.

Summary

1. The action of zinc chloride and hydrochloric acid on *n*-amyl alcohol produces *n*-amyl chloride in 57% yield and 10% of a mixture of 2- and 3-chloropentanes.

2. The action of zinc chloride and hydrochloric acid on *n*-amyl chloride yields 3% of a mixture of 2- and 3-chloropentanes.

3. The action of thionyl chloride on *n*-amyl alcohol in pyridine gives *n*-amyl chloride in 80% yield with no rearranged products.

4. A corrected refractive index for *n*-amyl chloride, free of traces of 2- and 3-chloropentanes, is recorded.

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[12] The microscopic analysis was completed by Dr. E. F. Williams of the Department of Minerology, The Pennsylvania State College.

[13] Darzens, *Compt. rend.*, **152**, 1314 (1911).

5. The action of sulfuric acid and hydrobromic acid on *n*-butyl alcohol gives no rearranged bromide.

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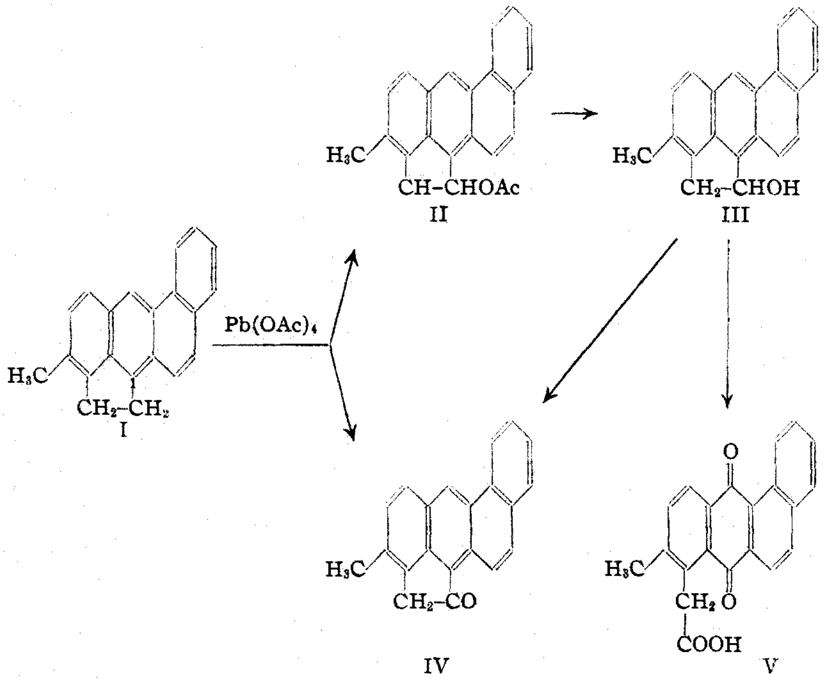
The Oxidation of Methylcholanthrene and 3,4-Benzpyrene with Lead Tetraacetate; Further Derivatives of 3,4-Benzpyrene

BY LOUIS F. FIESER AND E. B. HERSHBERG[1]

In a recent paper[2] we reported that on treatment with lead tetraacetate 1,2-benzanthracene is converted into the 10-acetoxy derivative, 10-methyl-1,2-benzanthracene is attacked in the methyl group giving 10-acetoxymethyl-1,2-benzanthracene, and 1,2,5,6-dibenzanthracene is more resistant to oxidation by the reagent and under comparable conditions is largely recovered unchanged. This specific oxidation reaction provides a means of distinguishing between hydrocarbons of varying degrees of reactivity and of locating a reactive center in a hydrocarbon molecule whether this is in an aromatic nucleus or a side chain. Thus far nuclear oxidation by the reagent has been observed only in the case of the *meso*-acetoxylation of anthracene[3] and 1,2-benzanthracene,[2] and the known examples of the oxidation of an alkyl residue by lead tetraacetate all involve acetoxylation at an activated α-position in a side chain or side ring. The reaction with 10-methyl-1,2-benzanthracene[2] is one instance of the latter type of oxidation, and similar reactions have been observed with toluene,[4] acenaphthene,[5] and tetralin.[6]



On investigating methylcholanthrene and 3,4-benzpyrene, it was found that these powerfully carcinogenic hydrocarbons are highly susceptible to attack by lead tetraacetate. 3,4-Benzpyrene is oxidized rapidly at room temperature in acetic acid–benzene and converted in over 90% yield into a new monoacetoxy derivative. Methylcholanthrene is even more susceptible to attack and in the most satisfactory procedure, adopted because of the sensitivity of the reaction products, the oxidation was conducted under ice cooling. One reaction product, isolated only in small amounts when one equivalent of oxidizing agent was employed, is a rather sparingly soluble and high melting substance having the composition of a keto derivative of methylcholanthrene. The chief product was an acetoxy derivative, and on hydrolysis it gave a neutral alcohol. A relationship between the two substances was easily established, for the alcohol was found to yield the ketone on careful oxidation with sodium dichromate. Further oxidation with the same reagent gave a yellow anthraquinone (vat test) having an acidic group, and this proved to be identical with

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[1] Research Fellow on funds from the National Cancer Institute and the Eli Lilly Company.

[2] Fieser and Hershberg, THIS JOURNAL, **60**, 1893 (1938).

[3] K. H. Meyer, *Ann.*, **379**, 73 (1911).

[4] Dimroth and Schweizer, *Ber.*, **56**, 1375 (1923).

[5] Marquis, *Compt. rend.*, **182**, 1227 (1926).

[6] Criegee, *Ann.*, **481**, 263 (1930).