2,3,4,5-Tetramethylbenzyl Alcohol (XV).—The aldehyde (15 g.) was reduced by refluxing it for twelve hours in acetic acid (100 cc.) and water (30 cc.) with zinc dust (4 g.). During this time fresh zinc dust was added every two hours in 2-g. portions. The mixture was cooled and poured into water, which precipitated a mixture of the alcohol and its acetate. The oil was taken up in ether, washed with carbonate, dried and the solvent evaporated. There remained 15 g. of a mixture of the alcohol and acetate. A portion of this (2.5 g.) was refluxed for three hours with 20% sodium hydroxide solution (60 cc.). The solution was cooled, acidified with dilute sulfuric acid, extracted with ether and the ether layer was dried. Removal of the ether left an oil which solidified on cooling. After crystallization from petroleum ether, the substance (0.9 g.) was white and melted at 80–81°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.5; H, 9.75. Found: C, 80.6; H, 10.02.

2,3,4,5-Tetramethylbenzyl Chloride (XVI).—The crude mixture of alcohol and acetate (12.5 g.) was refluxed for six hours with concd. hydrochloric acid (215 cc.) and then allowed to stand overnight. The reaction mixture was poured into water and the oil was removed by extraction with ether. The ethereal solution was washed with dilute carbonate, then with water, and was dried. Removal of the ether left an oil which distilled at 139–140° under 15 mm. The yield was 6 g., while 3 g. of undistillable residue remained in the flask. The chloride solidified on cooling and after crystallization from alcohol, it melted at 44–45°.

Anal. Calcd. for $C_{11}H_{15}Cl$: C, 72.4; H, 8.28. Found: C, 72.8; H, 8.34.

2,3,4,5-Tetramethylbenzyl Cyanide (XVII).—The chloride (2 g.) in alcohol (15 cc.) was added to a boiling solution of sodium cyanide (0.89 g.) in water (2 cc.). The mixture was refluxed for three hours, then filtered and the alcohol was removed from the filtrate under reduced pressure. The brown solid was removed and crystallized twice from 50% alcohol (charcoal). The yield was 1 g., and the white plates melted at 57–58°.

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.2; H, 8.67. Found: C, 83.17; H, 8.12.

2,3,4,5-Tetramethylphenylacetic Acid (VI).—The nitrile (0.2 g.) was refluxed for one hour with 25% sulfuric acid (10 cc.). The mixture was poured into water, and the solid was removed and crystallized twice from dilute alcohol. It formed fine, colorless needles which melted at 159–160° and it was identical with the acid VI obtained by action of hydrobromic acid upon the product obtained from prehnitene and ethyl diazoacetate, as shown by the mixed melting point.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33. Found: C, 74.71; H, 8.28.

Claus and Föhlisch,[9] who synthesized this acid by oxidation of acetoprehnitene followed by reduction (hydriodic acid) of the α keto acid, reported that it melted at 125°, but these authors must have had a very impure specimen in hand.

Summary

1. When prehnitene and ethyl diazoacetate react at 140°, the product consists of a mixture of 2,3,4-trimethyldihydrocinnamic acid and 3,4,5,6-tetramethyl-Δ-1,3,6-cycloheptatrienecarboxylic acid.

2. The cycloheptatriene acid rearranges into 2,3,4,5-tetramethylphenylacetic acid when subjected to the action of hydrobromic acid in acetic acid.

3. The condensation was carried out in various ways in the attempt to detect or isolate norcaradiene and indazoline derivatives, the supposed primary products, but without success.

4. The structure of the trimethylhydrocinnamic acid and that of the tetramethylphenylacetic acid were proved by independent syntheses.

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[9] Claus and Föhlisch, *J. prakt. Chem.*, [2] 38, 230 (1888).

MINNEAPOLIS, MINN. RECEIVED DECEMBER 6, 1937

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Side Chain Bromination of Prehnitene and Some 2,3,6-Trimethylphenyl Derivatives[1]

BY LEE IRVIN SMITH AND COURTLAND L. AGRE

In the previous paper, the synthesis of 2,3,4-trimethyldihydrocinnamic acid was described. It was planned originally to synthesize this acid by starting with prehnitene (1,2,3,4-tetramethylbenzene) and converting the hydrocarbon into 2,3,4-trimethylbenzyl bromide by direct bromination at an elevated temperature in sunlight. Although a fair yield of a trimethylbenzyl bromide was obtained, the subsequent transformations of the substance showed that the methyl groups were not in positions 2, 3 and 4, but were in positions 2, 3 and 6. This interesting bromination of an interior methyl group in prehnitene makes readily accessible many 2,3,6-trimethylbenzyl derivatives in good yields, a number of which are described in the experimental part of this paper together with the proof of the orientation of the methyl groups. The compounds prepared, and

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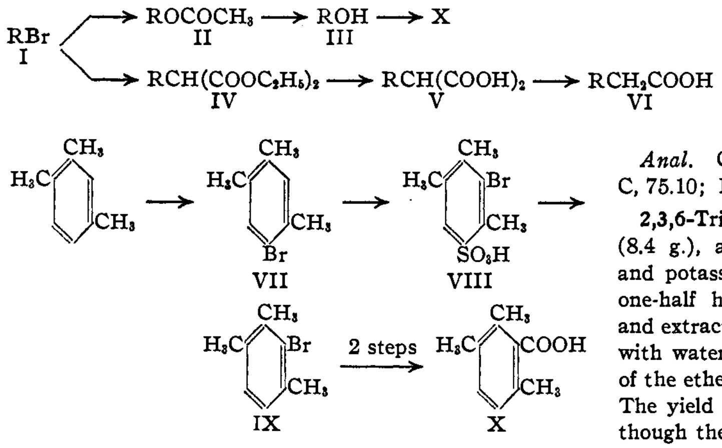
[1] Polymethylbenzenes. XXI. Paper XX, THIS JOURNAL, 60, 648 (1938).

their relationships, are shown in the chart (R = 2,3,6-trimethylbenzyl).



Experimental Part[2]

Bromination of Prehnitene: 2,3,6-Trimethylbenzyl Bromide (I).—Prehnitene (20 g.) was placed in a flask equipped with a dropping funnel and reflux condenser, and the apparatus was placed in direct sunlight. The temperature was brought to 140° and liquid bromine (25 g.) was added slowly during the course of one hour. The brown reaction product was washed with water, dried over sodium sulfate, and distilled. The distillate (13 g., 41%) was collected at 146° under 23 mm. (130–132° under 14 mm.).

Anal. Calcd. for $C_{10}H_{13}Br$: C, 56.35; H, 6.10. Found: C, 55.83; H, 5.66.

From the residue in the distilling flask a dibromide was isolated, which crystallized from alcohol–acetone in the form of white needles melting at 205°.

Anal. Calcd. for $C_{10}H_{12}Br_2$: C, 41.1; H, 4.1. Found: C, 41.5; H, 3.63.

Ethyl 2,3,6-Trimethylbenzylmalonate (IV).—The bromide I (4 g.) was added to a solution containing malonic ester (3 g.) in sodium ethoxide (0.43 g. sodium, 10 cc. absolute ethanol). After heating for one and one-half hours the mixture was diluted with water and extracted with ether. The ether solution was washed with water and dried over sodium sulfate. Evaporation of the ether left a yellow oil which was distilled. The distillate weighed 3.5 g. (64%), boiled at 186–189° under 10 mm. (207–209° under 24 mm.), and was water white.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.90; H, 8.22. Found: C, 69.87; H, 8.02.

2,3,6-Trimethylbenzylmalonic Acid (V).—The ester (3 g.) was refluxed for five hours with a solution of potassium hydroxide (4 g.) in water (13 cc.). The mixture was extracted with ether, the aqueous layer was acidified and again extracted with ether. The latter ethereal solution after washing and drying over sodium sulfate was evaporated. The white solid was crystallized from water (charcoal), and then from ether–petroleum ether. The acid melted at 143–144° (dec.).

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.15; H, 6.83. Found: C, 66.50; H, 6.86.

2,3,6-Trimethyldihydrocinnamic Acid (VI).—The malonic acid (200 mg.) was heated to 190°. Decarboxylation was rapid and complete, and the residue solidified on cooling. The product crystallized from water in the form of white needles which melted at 91–92°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.00; H, 8.39. Found: C, 75.10; H, 8.53.

2,3,6-Trimethylbenzyl Acetate (II).—The bromide I (8.4 g.), acetic anhydride (5 cc.), acetic acid (15 cc.) and potassium acetate (5 g.) were refluxed for two and one-half hours. The solution was diluted with water and extracted with ether. The ether solution was washed with water and dried over sodium sulfate. Evaporation of the ether left an oil which boiled at 152° under 23 mm. The yield was 5.5 g. (73%) of distilled material, but although the liquid boiled over a narrow range of temperature, it was not pure and a good analysis for carbon and hydrogen was not obtained.

2,3,6-Trimethylbenzyl Alcohol (III).—The acetate II (4 g.) was hydrolyzed by refluxing it for three hours with a solution of potassium hydroxide (3 g.) in water (20 cc.). The product was removed by extracting with ether, and the ether solution was washed and dried over sodium sulfate. Evaporation of the ether left a white solid, which after three crystallizations from petroleum ether melted at 83.5–85°.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33. Found: C, 79.49; H, 9.33.

2,3,6-Trimethylbenzoic Acid (X).—The alcohol III (270 mg.) was suspended in sodium hydroxide solution (1 *N*, 7 cc.) and shaken with potassium permanganate solution (300 mg. in 7 cc. of water) first for two and one-half hours at 0° and then for two hours at room temperature. The product, isolated in the usual way, was oily and contained a considerable amount of unchanged alcohol, and it was again oxidized as described above. The crude acid melted at 104–107°, but when recrystallized from water the substance formed white needles which melted at 110–111°. Lapworth and Wechsler[3] reported the melting point as 105–106°.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.17; H, 7.32. Found: C, 73.68; H, 7.51.

5-Bromopseudocumene (VII) was prepared by the direct bromination of the hydrocarbon according to the procedure of Smith and Moyle.[4]

3-Bromopseudocumene sulfonic acid-5 (VIII) was prepared from VII by means of the Jacobsen rearrangement[4] (p. 4). In this connection, the direct bromination of pseudocumene-5-sodium sulfonate which was stated by Smith and Moyle[4] (p. 8) to give 3-bromopseudocumene-5-sodium sulfonate, could not be duplicated although several modifications of the procedure of Smith and Moyle were tried. At present there is no explanation of the differences between the results obtained in the present work and those of Smith and Moyle.

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[2] Microanalyses by J. W. Opie.

[3] Lapworth and Wechsler, *J. Chem. Soc.*, **91**, 994 (1907).

[4] Smith and Moyle, THIS JOURNAL, **58**, 8 (1936).

3-Bromopseudocumene (IX) was obtained by hydrolysis of the sulfonic acid (VIII) with sulfuric acid at 150°. The yield was 80% and the product boiled at 94.5–95.5° under 8 mm.

2,3,6-Trimethylbenzoic Acid (X).—3-Bromopseudocumene (5 g.) was converted into the Grignard reagent by dissolving it in ethyl bromide (2.7 g.) and ether (25 cc.) and dropping the mixture slowly onto magnesium (2.4 g.) in an atmosphere of dry nitrogen. The Grignard reagent was carbonated by passing into it a stream of dry carbon dioxide until no further precipitate was formed. The acid, isolated in the usual way and crystallized from water, melted at 110.5–112°, alone and when mixed with the acid X prepared from prehnitene.

Summary

1. When brominated at 140° in direct sunlight and in the absence of a solvent, prehnitene forms 2,3,6-trimethylbenzyl bromide. A number of 2,3,6-trimethylbenzyl derivatives were prepared from this bromide, and the proof of the orientation of the methyl groups is given.

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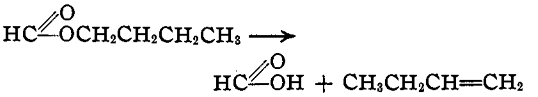
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Organic Reactions with Boron Fluoride.[1] XX. Acidolysis of Esters

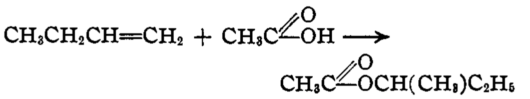
BY FRANK J. SOWA

It has been shown that esters[2] react with benzene through the intermediate olefin stage and also that olefins[3] and alcohols[4a] react with acids in the presence of boron fluoride.

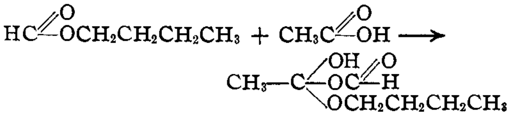
The purpose of this investigation was first to study the acidolysis of esters in the presence of boron fluoride and second to determine the course of the reaction. In studying the course of the reaction, it was necessary to determine whether it proceeded through the olefin stage as in equations (I) and (II) to give secondary alkyl esters, or by a mechanism that would not permit olefin formation as in equations (III) and (IV) to give normal alkyl esters.


I

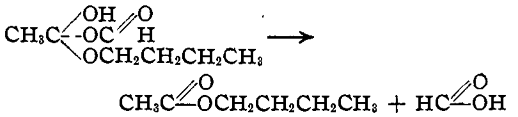
$$\mathrm{HC{\overset{O}{\diagup\!\!\!\!=}}OCH_2CH_2CH_2CH_3 \longrightarrow HC(=O)OH + CH_3CH_2CH{=}CH_2} \qquad \mathrm{I}$$


II

$$\mathrm{CH_3CH_2CH{=}CH_2 + CH_3C(=O)OH \longrightarrow CH_3C(=O)OCH(CH_3)C_2H_5} \qquad \mathrm{II}$$


III

$$\mathrm{HC(=O)OCH_2CH_2CH_2CH_3 + CH_3C(=O)OH \longrightarrow CH_3{-}C(OH)(OCH_2CH_2CH_2CH_3){-}OC(=O){-}H} \qquad \mathrm{III}$$


IV

$$\mathrm{CH_3C(OH)(OCH_2CH_2CH_2CH_3){-}OC(=O)H \longrightarrow CH_3C(=O)OCH_2CH_2CH_2CH_3 + HC(=O)OH} \qquad \mathrm{IV}$$

The effect of the quantity of boron fluoride upon the yield of the new ester and the relative efficiencies of sulfuric acid, zinc chloride, boron fluoride, and dihydroxyfluoboric acid as catalysts was also considered.

Experimental Part

Acidolysis Procedure.—The procedure was quite uniform throughout this study and will be described as a general method.

One half mole of an ester, 40 g. of acetic acid and 50 g. of the acetic acid–boron fluoride compound, $(CH_3COOH)_2 \cdot BF_3$, b. p. 142°, were weighed in a 200-cc. round-bottomed flask. The flask was fitted with a two-holed stopper into which was inserted a reflux condenser and a thermometer that extended into the liquid. The contents were heated to 100° on a constant temperature bath. At the end of one hour the reaction flask was cooled in an ice-bath while a solution of sodium carbonate was poured slowly through the top of the reflux condenser until the contents were neutral. The ester layer was separated, dried and carefully fractionated through an efficient 45-cm. Widmer column that was packed with glass beads in the inside tube.

When *n*-propyl esters were treated with acetic acid two fractions were collected, the first from 84 to 90° and the second from 98 to 102°. The first fraction collected from several runs was proved to be isopropyl acetate from its physical properties and by saponifying it to isopropyl alcohol which was further identified. In a similar manner the second fraction proved to be *n*-propyl acetate. By the acidolysis of the three esters, *n*-propyl propionate, benzoate and salicylate 3 g. (3%), 3.6 g. (4%) and 2 g. (2%), respectively, of isopropyl acetate and 40.8 g. (40%), 24.3 g. (24%) and 67.3 g.(66%) of *n*-propyl acetate were formed.

Similarly fractions boiling at 108–113° and 122–126° were proved to be the products *s*-butyl acetate and *n*-butyl acetate, respectively, when the esters *n*-butyl propionate, benzoate and salicylate were each treated with acetic acid as described above. *n*-Butyl propionate gave 4.6 g. (4%) of *s*-butyl and 50 g. (43%) of *n*-butyl acetate; *n*-butyl benzoate gave 5.8 g. (5%) of *s*-butyl and 80.1

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(1) For previous article see Dorris and Sowa, THIS JOURNAL, **60**, 358 (1938).

(2) McKenna and Sowa, *ibid.*, **59**, 1204 (1937).

(3) Dorris, Sowa and Nieuwland, *ibid.*, **56**, 2689 (1934).

(4) (a) Hinton and Nieuwland, *ibid.*, **54**, 2017 (1932); (b) Sowa and Nieuwland, *ibid.*, **58**, 271 (1936).