filtered, washed with water, and recrystallized from water in the presence of decolorizing carbon. A yield of 13.8 g. (65%) of 5-nitrovanillic acid as light yellow needles melting at 214–215° and not depressing a mixed melting point with authentic 5-nitrovanillic acid was obtained.

Reaction of Vanillic Acid with Nitric Acid.—A suspension of 5 g. of vanillic acid and several pieces of ice in 150 cc. of water was placed in a beaker surrounded by an ice-bath. While the temperature was maintained between 10 and 15°, 200 cc. of 1:1 nitric acid was stirred in. Very little reaction took place. After all the nitric acid was added, the mixture was warmed to 35°, at which temperature the white vanillic acid precipitate turned yellow in color. The yellow mixture was stirred at room temperature for one hour, and then poured into an excess of cold water. The bright yellow crystalline precipitate was filtered, washed with water, and dried in a vacuum desiccator. A yield of 6.3 g. of yellow crystals melting at 121–124° was obtained. Recrystallization from water yielded yellow needles melting at 123–124°, which did not depress a mixed melting point with authentic 4,6-dinitroguaiacol. The yield was substantially quantitative.

Summary

Vanillic acid has been prepared by oxidizing vanillin with alkali and one mole of silver nitrate and acidifying with sulfur dioxide. Non-reducing acids yielded, in addition, a small amount of 5-nitrovanillic acid. The mechanism of the formation of 5-nitrovanillic acid has been ascertained. 5-Nitrovanillic acid and 4,6-dinitroguaiacol have been prepared from vanillic acid.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

Syntheses of δ-Cyclopentyl-n-valeric Acid[1]

BY GEORGE H. COLEMAN, JOSEPH E. CALLEN AND CLINTON A. DORNFELD

In this Laboratory we recently had occasion to prepare a quantity of δ-cyclopentyl-*n*-valeric acid. Because the best method[2] previously reported, a six-step procedure starting from bromocyclopentane and involving Grignard reactions with ethylene oxide, gives an over-all yield of only 7–12%, and because a preliminary investigation of a three-step procedure[3] involving the reaction of cyclopentylmagnesium bromide with furfural was not encouraging, other methods of preparation were studied. Of these methods, two were finally used. One synthesis consisted of the following three steps: reaction of cyclopentylmagnesium bromide with γ-chloropropyl *p*-toluenesulfonate to yield γ-chloropropylcyclopentane, condensation with malonic ester to give ethyl γ-cyclopentylpropylmalonate, and hydrolysis and decarboxylation to δ-cyclopentyl-*n*-valeric acid. A yield of only 19% of γ-chloropropylcyclopentane was obtained in the first step although better results for this type of reaction have been reported.[4]

It was found more feasible to obtain the γ-halopropylcyclopentane required for the synthesis by another method involving the following two steps: reaction of cyclopentylmagnesium bromide with allyl bromide to form allylcyclopentane, and addition of hydrogen bromide in the presence of oxygen to give γ-bromopropylcyclopentane.[5] Allylcyclopentane was obtained by a modification of the method of Piaux and Bourguel.[6] A malonic ester synthesis with the γ-bromo compound resulted in δ-cyclopentyl-*n*-valeric acid in 29% over-all yield. The products obtained by the two methods were identical and corresponded in properties and derivatives to the literature values.

In the reaction of hydrogen bromide with allylcyclopentane there was formed in addition to γ-bromopropylcyclopentane some slightly lower boiling material, probably β-bromopropylcyclopentane. In several trial runs, benzoyl peroxide (one mole per cent.) was used to orient the entering hydrogen bromide, but oxygen was found to give equally good yields of the desired isomer.

In one of the preliminary runs, the bromopropylcyclopentane was not fractionated, but was carried directly through the malonic ester synthesis to the acid. The product was a mixture of acids from which the δ-cyclopentyl-*n*-valeric acid was obtained by a careful fractionation.

Experimental

γ-Chloropropylcyclopentane.—(*Cf.* ref. 4.) To a solution of cyclopentylmagnesium bromide, prepared from 100 g. (0.67 mole) of bromocyclopentane,[7] 16.3 g. (0.67 mole) of magnesium, and 300 ml. of dry ether, was added slowly 307 g. (1.23 moles) of γ-chloropropyl *p*-toluenesulfonate[4] with 500 ml. of dry ether, and the mixture was heated at reflux for twelve hours. The reaction mixture was decomposed with ice, and 6 *N* hydrochloric acid was added until the precipitate dissolved. The ether layer was separated and the aqueous layer extracted with ether. By fractional distillation of the combined ether extracts, 18.6 g. (19%) of γ-chloropropylcyclopentane was obtained, b. p. 83–87° (22.5 mm.), $n^{25}D$ 1.4582.

Allylcyclopentane.[6]—To a filtered solution of cyclopentylmagnesium bromide, prepared from 125 g. (5 moles) of magnesium, 745 g. (5 moles) of bromocyclopentane, and 3100 ml. of anhydrous ether, was added slowly with

(1) The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the State University of Iowa.

(2) Yohe and Adams, THIS JOURNAL, **50**, 1503 (1928).

(3) Katsnel'son and Kondakova, *Comp. rend. acad. sci. U. R. S. S.*, **17**, 367 (1937).

(4) Rossander and Marvel, THIS JOURNAL, **50**, 1491 (1928).

(5) Since this work was completed the preparation of γ-bromopropylcyclopentane by nearly the same method has been reported: Whitmore, Herr, Clark, Rowland and Schiessler, *ibid.*, **67**, 2059 (1945).

(6) Piaux and Bourguel, *Ann. chim.*, [11] **4**, 216 (1935).

(7) Noller and Adams, THIS JOURNAL, **48**, 1084 (1926).

stirring 605 g. (5 moles) of allyl bromide. During the addition of allyl bromide the reaction mixture was maintained at reflux temperature. After stirring for an additional two hours, the reaction mixture was cooled and the Grignard addition product decomposed with cold 6 *N* hydrochloric acid. The ether layer was separated, the aqueous layer extracted, and the combined extracts were dried and distilled; yield 387.5 g. (70.5%), b. p. 121–125° $n^{22}D$ 1.4398.

γ-Bromopropylcyclopentane.—Oxygen gas was bubbled into 693 g. (6.3 moles) of allylcyclopentane at 0° for thirty minutes with stirring. The passage of oxygen was continued, and hydrogen bromide[8] was passed in rapidly for three and one-half hours. At the end of this time, the theoretical amount and 52 g. in excess of hydrogen bromide had been absorbed. The reaction mixture was allowed to stand at 0° overnight, and the excess hydrogen bromide was distilled off at 50 mm. pressure. The mixture was washed with dilute carbonate solution, dried over anhydrous potassium carbonate, and distilled at atmospheric pressure through a partial take-off helices-packed column. More than 100 g. of lower boiling material distilled before the pure γ-bromopropylcyclopentane was collected at 204–207° (741 mm.), yield 786.3 g. The change in the index of refraction of the distillate was also used as an indication of the point at which to begin collection of the pure γ-bromopropylcyclopentane. This material was redistilled through a 70-cm. Vigreux column at reduced pressure before using; b. p. 99–100° (22 mm.), yield 714 g. (59.2%), $n^{25}D$ 1.4819.

Ethyl γ-Cyclopentylpropylmalonate.—(A) Alkylation of malonic ester was carried out in the usual manner[9] using 18.5 g. (0.126 mole) of γ-chloropropylcyclopentane and refluxing for sixteen hours; yield 22.4 g. (66%), b. p. 139–146° (2 mm.), $n^{25}D$ 1.4470. (B) In the same manner the malonic ester synthesis was carried out using 713 g. (3.73 moles) of γ-bromopropylcyclopentane and refluxing for thirteen hours; yield 839 g. (83%), b. p. 138–144° (2 mm.), $n^{25}D$ 1.4470.

δ-Cyclopentyl-*n*-valeric Acid.—Hydrolysis and decarboxylation of the ethyl γ-cyclopentylpropylmalonate was carried out according to the general method of "Organic Syntheses"[10] except that the oily layer of crude organic acid was separated in a funnel and the aqueous solution extracted with ether or benzene instead of using an automatic separator. (A) From 22.4 g. (0.08 mole) of γ-cyclopentylpropylmalonic ester, prepared as indicated in (A) above, was obtained 12.4 g. (84%) of δ-cyclopentyl-*n*-valeric acid; b. p. 137–137.5° (4.5 mm.), m. p. 12.5–14°, $n^{20}D$ 1.4596; m. p. of amide derivative after one recrystallization, 135–136° (uncor.). (B) From 838 g. (3.1 moles) of γ-cyclopentylpropylmalonic ester, prepared as indicated in (B) above, was obtained 448.8 g. (85%) of δ-cyclopentyl-*n*-valeric acid; b. p. 149–150° (9 mm.), m. p. 14–15, $n^{20}D$ 1.4595; m. p. of amide after one recrystallization 135–136° (uncor.).

In one run a mixture of cyclopentylvaleric acids prepared from an unfractionated bromopropylcyclopentane product was separated by careful fractionation through a 12-in. helices-packed partial take-off column: the fractions boiling 159–164° (19 mm.) ($n^{20}D$ 1.4587 to 1.4592) were rejected as probably containing a high percentage of the undesired isomer, and δ-cyclopentyl-*n*-valeric acid was collected at 164–165° (19 mm.), $n^{20}D$ 1.4594. None of the fractions boiling 159–164° (19 mm.) solidified upon cooling to 0°.

(8) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 338.

(9) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 250.

(10) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 416.

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Summary

δ-Cyclopentyl-*n*-valeric acid was prepared through a malonic ester synthesis from γ-bromopropylcyclopentane and from γ-chloropropylcyclopentane.

The γ-bromopropylcyclopentane was prepared by the addition of hydrogen bromide in the presence of oxygen to allylcyclopentane. The chloro compound was prepared by the alkylation of γ-chloropropyl *p*-toluenesulfonate with cyclopentylmagnesium bromide. In view of the respective yields, synthesis through the bromo compound was preferable.

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

The Skraup Reaction with *p*-Methoxyacetanilide

BY C. E. KASLOW AND SAMUEL RAYMOND[1]

The preparation of 6-methoxyquinoline from *p*-anisidine by the Skraup reaction is well-known. By using the modification of Manske[2] the yield of 6-methoxyquinoline has been increased and by using an improved method of isolation it has been shown that an important side reaction is the formation of 6-quinolinol, which may amount to as much as one-third of the product. It is probable that this compound is formed by demethylation of 6-methoxyquinoline, since the yield of the quinolinol increases with time at the expense of the 6-methoxyquinoline.

Sucharda and Mazonski[3] have reported that 6-quinolinol is a by-product in the Skraup method for preparation of quinoline itself. Its formation was ascribed to reduction of the nitrobenzene to phenylhydroxylamine which rearranges to *p*-aminophenol. The latter substance then undergoes a Skraup reaction yielding 6-quinolinol. A corresponding substance, 6-methoxy-8-hydroxy- or 6,8-dihydroxyquinoline, could not be isolated in the present case. The yields are recorded in Table I.

(1) The William S. Merrell Company Post Doctorate Research Fellow, 1945–1946.

(2) Manske, Ieger and Gallagher, *Can. J. Research*, **19B**, 318 (1941).

(3) Sucharda and Mazonski, *Ber.*, **69**, 2719 (1936).

Experimental

The following procedure was used for the preparation and isolation of 6-methoxyquinoline and 6-quinolinol.

6-Methoxyquinoline and 6-Quinolinol.—A mixture of 120 g. of anhydrous glycerol, 30 g. of boric acid, 36 g. (0.225 mole) of *p*-methoxyacetanilide, and 22 g. (0.14 mole) of *p*-nitroanisole was heated in a three-necked 500-ml. flask, fitted with a mechanical stirrer in an oil-bath