appreciated from the behavior of an end fraction representing 18% of the starting material and melting at 194.5–195.5°. By rechromatographing on alumina, seven successive fractions were obtained having the following melting points: 196.5–201°, 193–209°, 199–218°, 200.5–222°, 200–219°, 200–221.5°, 206–224°.

Acknowledgment.—We are indebted to Mr. William C. Alford and his assistants for the microanalyses herein reported; also to Dr. Nathan B. Eddy under whose direction the pharmacological properties of 6-methylcodeine were determined.

Summary

The preparation of 6-methylcodeine by the action of methyllithium on codeinone and also its chemical properties and degradation are described.

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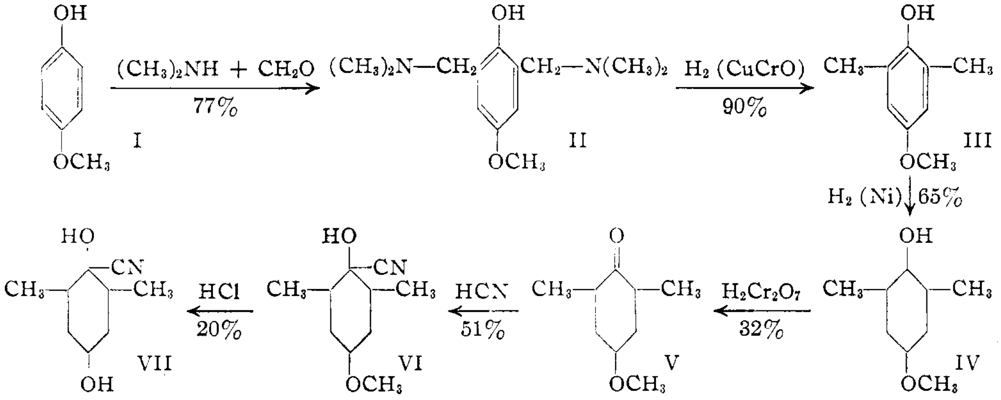
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MARYLAND]

Preparation and Reactions of 2,6-Dimethyl-4-methoxycyclohexanone

BY WILKINS REEVE AND ALEXANDER SADLE

The preparation and reactions of 2,6-dimethyl-4-methoxycyclohexanone cyanohydrin (VI) have been studied with the object of using this material as an intermediate in the synthesis of substituted cyclohexadienes.



Hydroquinone monomethyl ether (I) has been reported to react with dimethylamine and formaldehyde to form a mono-Mannich base.[1]

We have found that under more drastic conditions a di-Mannich base (II) may also be obtained in good yields. The condensation proceeds exclusively at the two and the six positions. The di-Mannich base undergoes hydrogenolysis to 2,6-dimethyl-4-methoxyphenol (III) in good yield. This represents a new and more practical synthesis of this material. The physical properties of this product agree with those reported in the literature.[2] The presence of the two methyl groups in the positions ortho to the phenolic group can be demonstrated by attempting to couple the material with diazotized *p*-toluidine; no colored product can be obtained. Furthermore, the methoxy group can be hydrolyzed with concentrated hydrogen bromide to give 2,6-dimethylhydroquinone. This latter compound has previously been made by methods which established its structure beyond all doubt.[3,4]

Hydrogenation of the 2,6-dimethyl-4-methoxyphenol yielded the previously unreported 2,6-dimethyl-4-methoxycyclohexanol (IV). This was oxidized to 2,6-dimethyl-4-methoxycyclohexanone (V). The oxidation proceeded in an anomalous manner in that after part of the alcohol had been oxidized, the reaction seemed to stop. There was no evidence of further reaction on the addition of more alcohol, even though the chromic acid was present in threefold excess.

Although attempts to prepare the cyanohydrin of 2,6-dimethylcyclohexanone have been reported[5] unsuccessful, 2,6-dimethyl-4-methoxycyclohexanone (V) rapidly adds hydrogen cyanide in an ethanol solution containing a little potassium cyanide.

The cyanohydrin groups of 2,6-dimethyl-4-methoxycyclohexanone cyanohydrin are resistant to attack by acids. After refluxing for two hours with concentrated hydrochloric acid, the only material which could be isolated was the 2,6-dimethyl-4-hydroxycyclohexanone cyanohydrin (VII) in a 6% yield. Heating with alcoholic hydrogen chloride for two hours at 100° also yielded the 2,6-dimethyl-

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(1) Decombe, *Compt. rend.*, **197**, 258 (1933).

(2) Bamberger, *Ber.*, **36**, 2040 (1903).

(3) Noelting and Bauman, *ibid.*, **18**, 1151 (1885).

(4) Jones and Kenner, *J. Chem. Soc.*, 1842 (1931).

(5) Noyes, *Am. Chem. J.*, **20**, 789 (1898).

4-hydroxycyclohexanone cyanohydrin in 20% yield and none of the expected ethyl esters resulting from the hydrolysis of the nitrile group. A similar unreactivity of a cyanohydrin group has been reported by von Auwers and Marburg[6] for the cyanohydrin of 2-methylcyclohexanone.

On heating with dilute alkali, the cyanohydrin (VI) dissociates into the ketone and cyanide ion, as shown by a positive Prussian blue test. When pure, small amounts of the cyanohydrin can be distilled. In general, however, the material decomposes on heating under reduced pressure and the ketone is recovered. When attempts were made to hydrolyze the methoxy group by heating with acetic anhydride and sulfuric acid,[7] only the acetate of the cyanohydrin was isolated. An attempted ether cleavage with anhydrous oxalic acid[8] was also unsuccessful.

Experimental[8a]

2,6-Bis-(dimethylaminomethyl)-4-methoxyphenol (II) was prepared by adding 341 g. (4.2 moles) of 37% formaldehyde over an hour period to 447 g. (3.6 moles) technical hydroquinone monomethyl ether and 1620 g. (9 moles) of a 25% solution of dimethylamine maintained at 15-20° with an ice-bath. The reaction mixture was stirred another hour with the ice-bath removed, then refluxed gently and another equal amount of formaldehyde added dropwise. Stirring and refluxing were continued forty-five minutes, and the reaction mixture then cooled to 10°. The top aqueous layer was separated, washed with 500 ml. of benzene and the benzene extract combined with the bottom layer of the reaction mixture. The benzene was washed twice with water, dried over anhydrous magnesium sulfate, and distilled under diminished pressure in a nitrogen atmosphere. There was obtained 655 g. (77% yield) of crude liquid material, b. p. 143° (3 mm.) to 152° (3.6 mm.).

2-Dimethylaminomethyl-4-methoxyphenol, previously prepared by Decombe[1] and reported to be an oil, was obtained in crystalline form. The material was prepared by Caldwell and Thompson's procedure[9] and a sample of the distilled material cooled in a Dry Ice-acetone-bath and allowed to warm up slowly. A solid was obtained which after recrystallization from 60-80° petroleum ether melted at 50-51°. *Anal.* Calcd. for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34. Found: C, 66.43; H, 8.39.

2,6-Dimethyl-4-methoxyphenol (III) was prepared by the hydrogenolysis of 614 g. of II dissolved in 340 ml. of dioxane (purified by refluxing over sodium) over 62 g. of copper chromite catalyst[10] at 235° and 275 atmospheres starting pressure of hydrogen at room temperature. Approximately two hours were required. There was obtained 354 g. (90% yield) of material distilling from 81 to 96° (1-2 mm.). The crude material was purified by steam distillation, m. p. 77° in agreement with the reported value.[2] *Anal.* Calcd. for $C_9H_{12}O_2$: $-OCH_3$, 20.40. Found: $-OCH_3$, 20.47. The **3,5-dinitrobenzoate** was prepared by the procedure of Phillips and Keenan,[11] m. p. 176-178° after recrystallization from 95% ethanol. *Anal.* Calcd. for $C_{16}H_{14}O_7N_2$: C, 55.49; H, 4.08; N, 8.09. Found: C, 55.33; H, 4.30; N (Dumas), 8.02. **2,6-Dimethylhydroquinone** was prepared from III by refluxing 0.5 g. with 10 ml. of 48% hydrobromic acid. The solid, which separated on cooling the reaction mixture was recrystallized from xylene and melted at 149-151° in agreement with the reported value.[3]

2-Methyl-4-methoxyphenol was prepared in a manner analogous to III from 2-dimethylaminomethyl-4-methoxyphenol. The m. p. was 70.5° after two recrystallizations from 60-80° petroleum ether, in agreement with the literature value.[12] *Anal.* Calcd. for $C_8H_{10}O_2$: $-OCH_3$, 22.46. Found: $-OCH_3$, 22.58.

2,6-Dimethyl-4-methoxycyclohexanol (IV) was prepared by the hydrogenation of 775 g. of III (partially purified by vacuum distillation only) dissolved in 600 ml. of cyclohexane (purified by refluxing over Raney nickel) over 80 g. of Raney nickel at 190° and a pressure of hydrogen at this temperature of 200 to 400 atmospheres. The reaction proceeded slowly; forty-three hours were required. There was obtained 126 g. of low boiling liquid, probably mostly 2-methyl-4-methoxycyclohexanol, and 527 g. (65% yield) of IV, b. p. 59° (1.2 mm.) to 80° (1.8 mm.), n^{25}_{D} 1.4622. *Anal.* Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 68.27; H, 11.42. The **3,5-dinitrobenzoate** was prepared in the usual way, m. p. 174-176° after recrystallization from 60-80° petroleum ether. *Anal.* Calcd. for $C_{16}H_{20}O_7N_2$: C, 54.54; H, 5.72; N, 7.95. Found: C, 54.77; H, 5.74; N (Dumas), 7.91. In a small run with III purified by steam distillation, the reaction was complete in six hours, and a somewhat higher yield was obtained.

2,6-Dimethyl-4-methoxycyclohexanone (V) was prepared by the oxidation of 342 g. (2.16 moles) of IV added slowly to 440 g. (1.5 moles) of technical potassium dichromate in 2715 ml. of water to which 202 ml. (3.7 moles) of concentrated sulfuric acid had been added. The temperature was maintained between 55 and 63°. After approximately half the alcohol had been added, there seemed to be no further evolution of heat. The reaction mixture was stirred at 50-60° for an additional two hours, cooled and extracted with ether. The ether extract was washed repeatedly with dilute sodium hydroxide solution, dried and distilled. The crude material (250 g.) on fractionation through a 60-cm. helices packed column gave 107 g. (32% yield) of ketone (V), b. p. 106-111° (24 mm.), $n^{27.5}_{D}$ 1.4520; and 88 g. of recovered alcohol (IV), b. p. 119-124° (24 mm.). *Anal.* Calcd. for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 69.30; H, 10.60. The use of twice as much potassium dichromate and a reaction temperature of 70° gave a 26% yield of V. The material, which still contained traces of the alcohol, was also characterized by its reaction with hydrogen cyanide and with dinitrophenylhydrazine. The **2,4-dinitrophenylhydrazone** was prepared from a solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid and recrystallized from 60-80° petroleum ether, m. p. 78.5-80°. *Anal.* Calcd. for $C_{15}H_{20}O_5N_4$: C, 53.56; H, 5.99; N, 16.66. Found: C, 53.28; H, 6.05; N, 16.77.

2,6-Dimethyl-4-methoxycyclohexanone cyanohydrin (VI) was prepared by adding 43 g. (0.28 mole) of V dissolved in 50 ml. of 95% ethanol to 8.3 g. (0.3 mole) of hydrogen cyanide and 0.3 g. of potassium cyanide dissolved in 14 ml. of 95% ethanol at 0° over a thirty-minute period. After the addition was complete, the ice-bath was removed and the mixture stirred for an additional thirty minutes. Fifteen drops of concentrated hydrochloric acid, 200 ml. of ether and 20 ml. of water were added. The water was removed from the resulting clear homogeneous solution by adding small amounts of anhydrous calcium chloride and separating the layers obtained. After drying the ether solution with anhydrous magnesium sulfate, the ether was removed by distillation at water-pump pressure and at a temperature not higher than 50°. The residue (50 g.) slowly crystallized over a period of two days when kept in a refrigerator. This crude cyanohydrin (26 g., 51% yield) could be crystallized from water and also from 60-

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(6) v. Auwers and Marburg, *Ber.*, **48**, 1389 (1915).

(7) Chitwood and Freure, THIS JOURNAL, **68**, 680 (1946).

(8) Waser and Sander, *Helv. Chim. Acta*, **8**, 106 (1925).

(8a) All melting points are uncorrected. Analyses are by Miss Eleanor Werble, Mrs. Mary Aldridge and Mr. Byron Baer of these laboratories.

(9) Caldwell and Thompson, THIS JOURNAL, **61**, 765 (1939).

(10) Prepared by slight modification of Adkin's method, Lazier and Arnold, "Organic Synthesis," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 144, note 11.

(11) Phillips and Keenan, THIS JOURNAL, **53**, 1924 (1931).

(12) Bamberger and Blangey, *Ann.*, **390**, 173 (1912).

80° petroleum ether. The pure material melted at 99.5–100.5° after two recrystallizations from petroleum ether. *Anal.* Calcd. for $C_{10}H_{17}O_2N$: C, 65.57; H, 9.38; N, 7.65. Found: C, 65.98; H, 9.36; N (Dumas), 7.66. Attempts to hydrolyze this cyanohydrin by the procedure given for phenylacetonitrile (use of hydrogen chloride dissolved in alcohol)[13] gave only a few per cent. of recovered cyanohydrin.

4-Hydroxy-2,6-dimethylcyclohexanone cyanohydrin (VII) was prepared in 20% yield from 5.6 g. of VI in 20 ml. of 95% ethanol saturated with hydrogen chloride by allowing the reaction mixture to stand overnight, removing the ammonium chloride by filtration, and then heating the filtrate in a sealed tube on the steam-bath for two hours. The reaction mixture was concentrated to a sirup, dissolved in a few ml. of water and an unidentified halogen containing solid, m. p. 170–175°, filtered off. Dropwise addition of 10% sodium hydroxide solution to the filtrate precipitated the dihydroxy compound, m. p. 169–171° after recrystallization from 60–80° petroleum ether. *Anal.* Calcd. for $C_9H_{15}O_2N$: C, 63.88; H, 8.92; N, 8.27. Found: C, 63.82; H, 9.15, N (Dumas), 8.41. Heating VII with dilute sodium hydroxide solution and ferrous ammonium sulfate followed by acidification gave a strong Prussian blue test.

Heating VI with five times its weight of concentrated hydrochloric acid on a steam-bath two hours gave 25% of unchanged VI and 6% of VII, isolated as above. The use of 48% hydrobromic acid gave erratic results.

1-Acetyl-2,6-dimethyl-4-methoxycyclohexanone cyanohydrin was prepared by mixing 12.1 g. of VI, 50 ml. of acetic anhydride and 1 ml. of concentrated sulfuric acid and refluxing for three hours. The reaction mixture was diluted with water, neutralized with sodium acetate and potassium carbonate, extracted with ether, and the ether layer dried with potassium carbonate and distilled. There was obtained 6 g. (40% yield) of the acetoxy compound, b. p. 103–107° (1.5 mm.). The material was inert to bromine dissolved in carbon tetrachloride and to aqueous potassium permanganate solution. Heating with sodium hydroxide solution and a ferrous salt followed by acidification gave a Prussian blue test. *Anal.* Calcd. for $C_{12}H_{19}O_3N$: C, 63.97; H, 8.50; $-OCH_3$, 13.77. Found: C, 64.04; H, 8.30; $-OCH_3$, 13.62.

Summary

Hydroquinone monomethyl ether can be converted into 2,6-dimethyl-4-methoxyphenol, the corresponding 2,6-dimethyl-4-methoxycyclohexanol and 2,6-dimethyl-4-methoxycyclohexanone, and the cyanohydrin of the latter. The cyanohydrin forms readily in spite of the methyl groups adjacent to the carbonyl group.

COLLEGE PARK, MD. RECEIVED JANUARY 21, 1950

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[13] Kimball, Jefferson and Pike, ref. 10, p. 284.

[CONTRIBUTION FROM THE CHEMICAL DIVISION OF THE PROCTER & GAMBLE CO.]

The Polymorphism of Synthetic and Natural 2-Oleyldipalmitin

BY E. S. LUTTON AND F. L. JACKSON

Introduction

Oleyldipalmitin and oleyldistearin have been isolated from various vegetable oils. In several cases it has been indicated that these glycerides were symmetrical, *i. e.*, 2-oleyldistearin (SOS)[1,2,3] and 2-oleyldipalmitin (POP).[4,5] A comparative polymorphic study of synthetic and natural SOS by X-ray and thermal techniques has been reported.[3] The present paper describes a similar study for POP.

Since the completion of this work, the polymorphism of SOS and POP, among other glycerides, has been discussed by Malkin, *et al.*[6] The results differ in important respects from those obtained in this Laboratory.

Experimental

Synthesis of POP.—The synthesis of POP was carried out by recognized procedure, namely, reaction of 1,3-dipalmitin with oleyl chloride in the presence of pyridine. The reaction product was purified by six crystallizations, four from alcohol–ether mixtures and two from Skellysolve B. Final yield of POP was 76%. Table I gives analytical constants for starting materials and product.

TABLE I

ANALYTICAL CONSTANTS FOR STARTING MATERIALS AND PRODUCT

Material	M. p., °C.	Saponifcn. value Exptl.	Saponifcn. value Theory	Hydroxyl value Exptl.	Hydroxyl value Theory	Iodine value Exptl.	Iodine value Theory
1,3-Dipalmitin	72.8	197.4	197.2	99	98.6	0.0	0.0
Methyl oleate	..	189.3	189.3	..	..	84.2	85.6
POP	38.3	...	...	..	..	30.6	30.5

Isolation of Natural POP from Stillingia Tallow.—A sample of stillingia tallow was obtained from Irving R. Boody and Co., Inc., New York, N. Y. It showed an acid value of 0.5 and iodine value of 56, the high I. V. being evidence of some admixture of stillingia oil, which however, introduced no difficulty in the separation of POP. A 500-g. portion of the tallow was crystallized from acetone (1:5) at 21°, and the 11% of largely trisaturated precipitate was discarded. A 16° precipitate representing 45% of the sample was largely disaturated. Three more crystallizations of this fraction at 16° yielded 25% of "natural POP," iodine value 30.0 and complete m. p. 36.9°.

Isolation of Natural POP from Piquia Fat.—Twenty pounds of piquia nuts were obtained from Boody and Co. After shelling, there were twelve pounds of hard pericarp and kernel which were crushed; large fibers were separated. Since pericarp and kernel fat are reported to be very similar, no further separation of nut portions was made. The fat bearing portions were extracted with warm hexane. (Innumerable spines in the pericarp introduce difficulties.) After Wesson refining of the extracted glycerides, there was 430 g. of dark fat. This was fractionally crystallized as in the case of stillingia tallow. A total of 0.25% of higher melting material (largely trisaturated) was removed at 21 and 16°. At 10°, 46% of largely disaturated glycerides was obtained. Two further crystallizations of this fraction at 16° gave 31% of another "natural POP," iodine value 29.8, complete m. p. 36.9°.

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[1] Meara, *J. Chem. Soc.*, 22 (1945).

[2] Filer, *et al.*, THIS JOURNAL, **68**, 167 (1946).

[3] Lutton, *ibid.*, **68**, 676 (1946).

[4] Hilditch, "Chemical Constitution of Natural Fats," 2nd Ed., 1947, p. 281.

[5] Meara, *J. Chem. Soc.*, 773 (1947).

[6] Malkin and Wilson, *ibid.*, 369 (1949).