[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, NATIONAL MEDICAL COLLEGE OF SHANGHAI

Synthesis of Pentyl- and Hexyl-α-naphthol

BY YUOH-FONG CHI AND CHERNG-TSUN JANG[1]

In this short paper are described methods of synthesizing 2-*n*-pentyl-, 2-isopentyl- and 2-*n*-hexyl-α-naphthols, which promise to have practical value as antiseptics. These compounds are formed by reducing 2-*n*-pentanoyl-, 2-isopentanoyl- and 2-*n*-caproyl-α-naphthols, which are in turn obtained by heating α-naphthol with *n*-valerianic, isovalerianic and *n*-caproic acids in the presence of zinc chloride.

α-Naphthol condenses with glacial acetic acid in the presence of acetic anhydride and zinc chloride giving 2-acetyl-α-naphthol.[2,3] It is also noted that α-naphthol condenses normally with propionic acid and *n*-butyric acid, giving 2-propionyl- and 2-*n*-butyl-α-naphthol, respectively.[4,5] The authors now find that α-naphthol reacts likewise with *n*-valerianic, isovalerianic and *n*-caproic acids giving in each case 2-*n*-pentanoyl-α-naphthol, 2-isopentanoyl-α-naphthol and 2-*n*-caproyl-α-naphthol, respectively.

The hydroxy ketones, such as 2-propionyl- and 2-*n*-butyryl-α-naphthols, have been shown to undergo reduction to their corresponding alkyl derivatives[5] by digesting with zinc amalgam in strong hydrochloric acid. In like manner, 2-*n*-pentanoyl-, 2-isopentanoyl- and 2-*n*-caproyl-α-naphthols are reduced to 2-*n*-pentyl-, 2-isopentyl- and 2-*n*-hexyl-α-naphthols, respectively, according to the well-known Clemmensen method of reduction.

Experimental Part

I. Condensation of *n*-Valerianic, Isovalerianic and *n*-Caproic Acids with α-Naphthol to Form the Corresponding Acylnaphthol Derivatives.—The general experimental procedure was to digest 27.2 g. of fused zinc chloride with the respective fatty acid (20–23 g.) until all zinc chloride had been dissolved. After cooling, 14.4 g. of α-naphthol was then added to the above solution, and digested for five minutes. The mixture, while still warm, was then poured into about 240 cc. of cold water with frequent stirring, whereupon an oil separated which finally solidified. This was extracted with benzene. After removal of the benzene an oil was obtained, from which the desired ketone was obtained by fractional distillation under reduced pressure (see Table I).

II. Formation of the Alkylated α-Naphthols.—Reduction of the above ketone derivatives of α-naphthol was accomplished easily by digestion with zinc amalgam according to the Clemmensen technique. The reduced products were extracted from the reduction media by benzene and purified by distillation under diminished pressure.

TABLE I

Ketone, -α-naphthol	B. p., °C.	Mm.	M. p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found		Hydrogen Calcd.	Hydrogen Found	
2-*n*-Pentanoyl	160–168	5	75.5–76.5	$C_{15}H_{16}O_2$	78.90	78.68	78.84	7.07	7.38	7.32
2-*i*-Pentanoyl	150–155	2	65 –66.5	$C_{15}H_{16}O_2$	78.90	78.47		7.07	7.46	7.38
2-*n*-Caproyl	180–186	5	62 –63	$C_{16}H_{18}O_2$	79.29	78.89	78.89	7.49	7.84	7.61

TABLE II

Alkylated α-naphthol	B. p., °C.	Mm.	M. p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found		Hydrogen Calcd.	Hydrogen Found	
2-*n*-Pentyl	130–135	5	45–46.5	$C_{15}H_{18}O$	84.06	84.34	84.50	8.41	8.38	8.39
2-*i*-Pentyl	135–140	3	. . .	$C_{15}H_{18}O$	84.06	84.10		8.41	8.10	
2-*n*-Hexyl	155–165	5	42–43	$C_{16}H_{20}O$	84.15	83.84	83.80	8.84	8.20	8.38

III. Oxime and Semicarbazone Derivatives of the Three Acyl-α-naphthol Compounds.—(Table III.)

TABLE III

-α-Naphthol	M. p., °C.	Formula	Nitrogen analyses, % Calcd.	Found	
		Oximes[a]			
2-*n*-Pentanoyl	115–117	$C_{15}H_{17}O_2N$	5.76	5.86	
2-*i*-Pentanoyl	149–151	$C_{15}H_{17}O_2N$	5.76	6.10	5.94
2-*n*-Caproyl	97– 99	$C_{16}H_{19}O_2N$	5.45	5.62	
		Semicarbazones[b]			
2-*n*-Pentanoyl	163–165	$C_{16}H_{19}O_3N_2$	14.74	14.42	
2-*i*-Pentanoyl	213–215	$C_{16}H_{19}O_2N_2$	14.74	14.20	
2-*n*-Caproyl	183–184	$C_{17}H_{21}O_3N_2$	14.05	14.14	

[a] The oximes were all purified by recrystallization from a mixture of benzene and petroleum ether. [b] The semicarbazones were purified by recrystallization from dilute ethanol.

Summary

1. α-Naphthol condenses with *n*-valerianic acid, isovalerianic acid and *n*-caproic acid, giving

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[1] The authors desire to express here their appreciation of the help from Professor Treat B. Johnson of Yale University in the revision of this report for publication.

[2] Witt, *Ber.*, **21**, 324 (1888).

[3] Witt and Braun, *ibid.*, **47**, 3219 (1914).

[4] Goldzweig and Kaiser, *J. prakt. Chem.*, [2] **43**, 95–97 (1891).

[5] Chi, THIS JOURNAL, **61**, 2487 (1939).

2-*n*-pentanoyl-α-naphthol, 2-isopentanoyl-α-naphthol and 2-*n*-caproyl-α-naphthol, respectively.

2. 2-*n*-Pentyl-α-naphthol, 2-isopentyl-α-naphthol and 2-*n*-hexyl-α-naphthol are obtained in each case by reduction of 2-*n*-pentanoyl-α-naphthol, 2-isopentanoyl-α-naphthol and 2-*n*-caproyl-α-naphthol according to Clemmensen's method.

3. The bacteriological properties of these new naphthols are now under investigation.

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Condensations. XVI. Various Acylations and Alkylations of the Sodium Enolates of Aliphatic Esters. Methods for the Syntheses of α,α-Disubstituted β-Keto Esters and of Certain Other Compounds[1]

BY BOYD E. HUDSON, JR., AND CHARLES R. HAUSER

The classical acetoacetic ester condensation of esters probably involves the acylation of the sodium enolate[2] of the ester; in the presence of sodium ethoxide a small portion of the ester is first converted into its sodium enolate which is then acylated by molecules of unchanged ester.[3] The scope of reactions of the sodium enolates of esters, however, was considerably limited until a base was found which would convert esters largely into their sodium enolates. In 1931 Schlenk, Hillemann and Rodloff[4] showed that sodium triphenylmethyl converts methyl diphenylacetate largely into its sodium enolate which could be acylated with acid chlorides or alkylated with alkyl halides. Since that time sodium triphenylmethyl has been used (mainly in this Laboratory) to effect certain acylations and alkylations of purely aliphatic esters. The present paper is a report of a more complete study of these types of reaction in which their preparative value is further demonstrated. Because of the increasing importance of sodium triphenylmethyl as a condensing agent a procedure is described for its preparation in approximately molar quantities. Also, the synthesis of a high grade of triphenylchloromethane (from which sodium triphenylmethyl is prepared) in kilogram quantities is described.

Preparation of Triphenylchloromethane.—The following procedure is a modification of the basic method of Gomberg[5] and employs a controlled hydrolysis of the reaction mixture making the use of large quantities of acetyl chloride unnecessary.[6]

A mixture of 2000 g. (2280 cc.) of dry thiophene-free benzene and 800 g. (500 cc.) of dry sulfur-free carbon tetrachloride was placed in a 5-liter three-necked flask equipped with a mercury-sealed mechanical stirrer and a reflux condenser, the latter being connected to a trap for the absorption of hydrogen chloride. The third neck of the flask was connected, by means of short pieces of 15-mm. glass and rubber tubing, to a 1-liter Erlenmeyer flask containing 600 g. (4.51 moles) of fresh resublimed aluminum chloride. The reaction flask (containing the benzene and carbon tetrachloride) was immersed in an ice-bath. The aluminum chloride was added to the reaction flask during a period of one and one-half to two hours, the reaction mixture not being allowed to reflux during the addition. Fifteen minutes after the addition of the aluminum chloride was complete, the reaction mixture was removed from the ice-bath. When spontaneous reaction ceased, the mixture was boiled until the evolution of hydrogen chloride subsided. The cooled product was then added to a vigorously stirred mixture of 1 liter of thiophene-free benzene and 2 liters of 6 *M* hydrochloric acid contained in a copper can (22.5 cm. diameter by 30 cm. deep) immersed two-thirds its depth in an ice-bath to maintain a reaction temperature not exceeding 25°. Stirring was continued for ten minutes longer. The benzene solution was decanted, 1 liter of ice-water was added to the aqueous layer and the diluted product extracted with one-half liter of benzene. The combined benzene solutions were washed with 250 cc. of concentrated hydrochloric acid and dried with calcium chloride. Solvent was distilled from the dried solution until the temperature of the residual solution reached 120°. The residue was then transferred to a 2-liter Erlenmeyer flask, cooled to about 40°, 25 cc. of acetyl chloride added and the mixture heated nearly to boiling. The solution was then cooled rapidly to room temperature, the crystallized triphenylchloromethane was crushed thoroughly and collected on a suction filter. The crystals were washed with two 300-cc. portions of ligroin (b. p. 70–90°) and dried *in vacuo* over mineral oil or paraffin; yield, 938 g.; m. p. 112–113° cor.; color, very light greenish-yellow. Concentration of the filtrate (solution temperature up to 110°) and

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[1] This paper has been constructed from portions of a Thesis presented by Boyd E. Hudson, Jr., in partial fulfillment of the requirements for the Ph.D. degree at Duke University.

[2] The sodium enolate of an ester is a salt, the anion of which is a resonance hybrid of keto and enol forms.

[3] (a) See Hauser and Renfrow, THIS JOURNAL, **59**, 1823 (1937); (b) Hauser, *ibid.*, **60**, 1957 (1938).

[4] Schlenk, Hillemann and Rodloff, *Ann.*, **487**, 135 (1931).

[5] Gomberg, *Ber.*, **33**, 3144 (1900).

[6] See Reynolds and Evans, THIS JOURNAL, **60**, 2559 (1938).