TABLE I

INFLUENCE OF TEMPERATURE AND CONDITION ON THE VELOCITY OF SUCROSE HYDROLYSIS BY INVERTASE

Reaction temp., °C.	20.2		−6.8		−6.8		−17.8	
Condition	Liquid		Liquid		Frozen		Frozen	
	min.	$k \times 10^5$	min.	$k \times 10^5$	min.	$k \times 10^5$	min.	$k \times 10^5$
	60	259.6	120	38.30	233	(35.80)	2,820	0.265
			410	39.62			7,200	.388
	120	255.6	1038	36.35	1038	10.54	10,080	.372
			1215	36.70	1218	10.62	17,280	.404
	240	273.8	1218	37.45	1563	10.32	20,160	.393
			1395	40.35			27,350	.201
	360	222.8	1740	40.60			28,970	.221
	Av.	253.0		38.5		10.49		.321

sis rather than by altering the physical characteristics of the solutions.

Summary

The velocity of invertase action in a frozen mixture at −6.8° was only 27% of that in a like mixture in the liquid state. The diminished availability of water may be responsible for this phenomenon.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE STATE COLLEGE OF WASHINGTON]

Some Derivatives of 2-Propionyl-1-naphthol

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Since the substitution of acyl and alkyl groups for nuclear hydrogen in phenols has given compounds with marked germicidal properties, we have extended our study in this field by preparing some derivatives of 2-propionyl-1-naphthol, with changes in side chain and nucleus.

We have compared methods of preparation of 2-propionyl-1-naphthol[1] and found little difference in yield, whether the process is carried out directly with α-naphthol or by intra-molecular rearrangement of the ester first formed through the action of the anhydride. However, the direct method requires fewer steps and we have been able to minimize the formation of purple by-products by the procedure given in the experimental part.

In attempting to prepare a di-acyl naphthol from 2-acetyl-1-naphthol by condensation with propionic acid, using zinc chloride as condensing agent, we obtained 2-propionyl-1-naphthol in good yield, the larger acyl group replacing the smaller. A similar replacement occurred when benzoic acid reacted with 2-acetyl-1-naphthol; however, the yield was very small. This replacement recalls the method of preparation of higher members of the salol series, by heating salol with eugenol or other phenols; the higher phenol replaces the lower.[2]

When examining some crystals of 2-propionyl-1-naphthol in subdued light, it was accidentally discovered that the compound shows marked triboluminescence, and this phenomenon persists whether the compound is dry or moistened with water or ethanol, even after removal of traces of impurities.

Reduction of acyl naphthols replaced the carbonyl oxygen by hydrogen and resulted in alkyl naphthols which showed an increase in germicidal activity. However, the pure reduced compounds on standing in the air slowly turned to brown oils and their preservation was difficult. It was anticipated that modification of the acyl side-chain might give compounds of greater stability, and such compounds have been made by condensation of the acyl group with aldehydes.[3] While there was marked reactivity with 2-propionyl-1-naphthol, we have been able to isolate only two derivatives in pure form. Acid condensing agents such as zinc chloride, aluminum chloride, or concentrated sulfuric acid produced marked color

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[1] Witt and Braun, *Ber.*, **47**, 3216 (1914); Fries, *ibid.*, **54**, 709 (1921); Stoughton, THIS JOURNAL, **57**, 204 (1935).

[2] German Patent 111,656; also May and Dyson, "The Chemistry of Synthetic Drugs," 4th edition, 1939, p. 219.

[3] Kostanecki, *Ber.*, **31**, 705 (1898); Pfeiffer, Kalckbrenner and Levin, *J. prakt. Chem.*, **119**, 109 (1928); Cheema, Gulati and Venkataraman, *J. Chem. Soc.*, 930 (1932).

changes and complex products, while potassium hydroxide in aqueous or alcoholic solution caused less polymerization. The lower temperatures tended to inhibit the Cannizzaro reaction, and also decreased the tendency to polymerization.

The ethers of acyl and alkyl naphthols which are reported were somewhat difficult to prepare, which is characteristic of ortho substituted naphthols. They are more stable than the naphthols when heated or exposed to air.

Experimental

2-Propionyl-1-naphthol.—We have carried out numerous trials of the methods reported by Goldzweig and Kaiser,[4] by Hantzsch[5] and by Stoughton[6] and obtained best yields from the following shortened modification of Hantzsch's method. Two hundred grams of fused zinc chloride was crushed and warmed with 300 g. of propionic acid until dissolved. To the warm solution was added 300 g. of α-naphthol and the mixture heated under reflux in an oil-bath to gentle boiling (145–150°) for forty to fifty minutes. The solution became orange, then bright red; if allowed to become deep red, an undue proportion of tar is formed. The mixture was allowed to cool slowly and to stand overnight, then gently warmed to 60° and diluted with an equal volume of warm glacial acetic acid. On standing overnight large yellow-green crystals separated from the purple solution, and were filtered with suction, rinsed by suspension in 200 g. of 85% acetic acid, filtered and recrystallized from hot ethanol. A second crop of crystals was obtained from the purple mother liquor by warming with activated carbon. The hot filtrate was cooled and diluted, and the crystalline product recrystallized from ethanol. The compound may be purified by solution in ethanol and 2% sodium hydroxide, which is then warmed with activated carbon, filtered and precipitated by neutralization with hydrochloric acid. The compound may also be purified by distillation *in vacuo*. A total yield of 200 g. was obtained; m. p. 81–82°.[7]

Crystals which were formed after melting and slowly cooling the dry compound gave the greatest brilliance of luminescence; when ground to a powder no further luminescence was observed.

2-Propionyl-1-ethoxynaphthalene.—Fifteen grams of 2-propionyl-1-naphthol and 75 ml. of ethanol were heated with a solution of 3 g. of sodium hydroxide in 10 ml. of water. This mixture was heated to gentle boiling under reflux and 8 g. of ethyl bromide was added drop by drop. After six hours of heating, 6 g. more of ethyl bromide was added and heating continued for six hours more. When a test with ferric chloride showed no coloration, the solution was cooled, neutralized and the brown oily product separated with ether, dried, and distilled *in vacuo*, giving a yellow viscous oil, b. p. 175–180° (15 mm.); yield, 13 g.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.85; H, 6.9. Found: C, 78.9; H, 7.0.

2-Propionyl-1-naphthol Phenylhydrazone.—Yellow plates from acetic acid, m. p. 136°.

Anal. Calcd. for $C_{19}H_{18}ON_2$: N, 9.65. Found: N, 9.36.

2-Propyl-1-naphthol.—Preparation by the Clemmensen reduction method as given in detail by Coulthard, Marshall and Pyman[9] and reported by Stoughton[10] required heating under reflux for twelve hours. The pale yellow oil, obtained by distillation *in vacuo*, solidified on standing and gradually turned brown; m. p. 48–50°. The germicidal activity of this compound has been tested recently and reported to be superior to that of 2-propionyl-1-naphthol.[11]

2-Propyl-1-ethoxynaphthalene.—Ten grams of 2-propyl-1-naphthol and 50 ml. of methyl ethyl ketone with 2 g. of sodium hydroxide were warmed, giving a brown solution. Fifteen g. of ethyl iodide was added in small portions and heating under reflux continued for a total of fifteen hours. The solvent was distilled off, the brown oil dissolved in ether, washed with 2% sodium hydroxide, and the ether layer separated, dried and distilled. The opaque red-brown liquid was distilled twice *in vacuo*, giving a pale yellow oil, b. p. 294–296° (690 mm.).

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.11; H, 8.41. Found: C, 83.9; H. 8.5.

2-Propyl-1-*n*-butyloxynaphthalene.—Ten grams of 2-propyl-1-naphthol was dissolved in 50 ml. of methyl ethyl ketone, and warmed with a solution of 2.1 g. of sodium hydroxide in 5 ml. of ethanol and 5 ml. of water. The solution turned deep green. Powdered copper, 0.1 g., was added as catalyst, and 10 g. of *n*-butyl bromide added in small portions. The solution was boiled under reflux for twenty-four hours, the solvents removed by distillation, and the brown oily residue was washed with 2% sodium hydroxide, extracted with ether, and the ether extract dried. Distillation *in vacuo* gave a pale yellow oil, b. p. 304–306° (692 mm.).

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.3; H, 9.01. Found: C, 84.0; H, 9.1.

4-Bromo-2-propionyl-1-naphthol.—Fifty grams of 2-propionyl-1-naphthol was dissolved in 125 ml. of chloroform; to this was added slowly and with vigorous stirring a solution of 50 g. of bromine in 125 ml. of chloroform. Large volumes of hydrobromic acid were given off. After standing for thirty minutes, the solution was washed with water by decantation until no longer acid. The chloroform layer was separated, the chloroform distilled off, and the yellow mass crystallized from ethanol. Yellow needles were obtained in nearly quantitative yield; m. p. and

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(4) Goldzweig and Kaiser, *J. prakt. Chem.*, **43**, 95 (1891).

(5) Hantzsch, *Ber.*, **39**, 3096 (1906).

(6) Stoughton, THIS JOURNAL, **57**, 202 (1935).

(7) On cooling an alcoholic solution of the compound, a crust of large transparent yellow-green plates formed. In dislodging these with a stirring rod, in a dark room, flashes of blue light were seen as the rod broke the mass of crystals beneath the mother liquor. This triboluminescence appeared when the compound was subjected to friction or to percussion, even after repeated recrystallization. The phenomenon persisted whether the crystals were dry or suspended in water or ethanol, and seemed to be an inherent property of the compound.[8]

(8) R. Ghigi, *Gazz. chim. ital.*, **57**, 278 (1927).

(9) Coulthard, Marshall and Pyman, *J. Chem. Soc.*, 280 (1930).

(10) Stoughton, THIS JOURNAL, **57**, 204 (1935).

(11) H. L. Cole, C. C. Prouty and Emily R. Meserve, THIS JOURNAL, **63**, 3523 (1941).

m. p. when mixed with a sample prepared by Hantzsch's method,[12] 98–99°.

4-Bromo-2-propionyl-1-ethoxynaphthalene.—A mixture of 5.6 g. of 4-bromo-2-propionyl-1-naphthol with 0.8 g. of sodium hydroxide in 4 ml. of water and 50 ml. of methyl ethyl ketone was heated, and 5 g. of ethyl bromide slowly added. After eight hours of heating under reflux, 3.0 g. more of ethyl bromide was added, and heating continued for a total of sixteen hours. The solvent was then distilled off, the residue washed and crystallized from ethanol, giving a yield of 3.8 g. of pale yellow needles, m. p. 68–69°.

Anal. Calcd. for $C_{15}H_{15}O_2Br$: Br, 26.03. Found: Br, 26.10.

4-Bromo-2-propionyl-1-*n*-propyloxynaphthalene.—A mixture of 15 g. of 4-bromo-2-propionyl-1-naphthol, 50 ml. of methyl ethyl ketone, and a solution of 2.2 g. of sodium hydroxide in 10 ml. of ethanol and 10 ml. of water was heated under reflux, and 12 g. of *n*-propyl bromide was added in small portions. After forty-eight hours of heating the solvent was distilled off, the oily layer taken up in ether and washed with 2% aqueous sodium hydroxide. The ethereal layer was separated, dried and distilled *in vacuo.* The light yellow oil had a slightly sweet odor; b. p. 298–303° (690 mm.).

Anal. Calcd. for $C_{16}H_{17}O_2Br$: Br, 24.90. Found: Br, 25.23.

4-Nitro-2-propionyl-1-naphthol.—Ten grams of 2-propionyl-1-naphthol was powdered and suspended in 200 ml. of 50% acetic acid. Ten ml. of concentrated nitric acid was diluted with 30 ml. of glacial acetic acid and added slowly to the vigorously stirred suspension. After five hours the mixture was diluted, filtered, and the solid crystallized from ethanol giving fine yellow needles, m. p. 162–163°.

Anal. Calcd. for $C_{13}H_{11}O_4N$: N, 5.7. Found: N, 5.5.

The phenylhydrazone crystallized from ethanol in pale brown crystals which melted at 199–200°.

Anal. Calcd. for $C_{19}H_{17}O_3N_3$: N, 12.53. Found: N, 12.02.

2-Propionyl-β-(2-chlorobenzylidene)-1-naphthol.—Five grams of 2-propionyl-1-naphthol and 5 g. of *o*-chlorobenzaldehyde were suspended in 25 ml. of ethanol, cooled to 0°, and vigorously stirred. A solution of 50 g. of potassium hydroxide in 35 ml. of water was added slowly during a period of one hour, and stirring at 0° continued for two hours, after which the mixture was allowed to stand at room temperature out of contact with air for two days. The dark red alcoholic solution was poured into 200 ml. of ice-water and neutralized with dilute hydrochloric acid. The yellow precipitate was filtered off and crystallized from hot ethanol. Long yellow needles were obtained which melted at 93–94°.

Anal. Calcd. for $C_{20}H_{15}O_2Cl$: Cl, 11.01. Found: Cl, 11.06.

4-Bromo-2-propionyl-β-(2-chlorobenzylidene)-1-naphthol.—Three grams of 4-bromo-2-propionyl-1-naphthol and 1.5 g. of *o*-chlorobenzaldehyde were dissolved in 25 ml. of 1,4-dioxane, cooled to 0°, and a solution of 30 g. of potassium hydroxide in 20 ml. of water, also cooled to 0°, was added slowly over a period of two hours, with vigorous mechanical stirring. The solution turned dark red and a precipitate formed. The mixture was allowed to stand for two days out of contact with air and at room temperature, then poured into 100 ml. of ice-water and neutralized with dilute hydrochloric acid. The yellow precipitate was filtered and crystallized from ethanol, giving light yellow needles which melted at 129°.

Anal. Calcd. for $C_{20}H_{14}O_2ClBr$: Cl and Br, 28.76. Found: Cl and Br, 28.5.

As typical of the reactivity of aromatic aldehydes in the presence of condensing agents, when 10 g. of 2-propionyl-1-naphthol and 5 g. of benzaldehyde were warmed with 5 g. of fused zinc chloride the viscous mass became yellow-brown at 70°, deepening in color as the temperature rose, until at 170° there was slight effervescence and the color changed to deep crimson. The temperature was held at 170° for about ten minutes or until effervescence ceased. Upon dilution a gray-blue granular precipitate separated which was dissolved in acetic acid giving a red solution. Fractional precipitation by dilution with water gave successive portions of the gray-blue precipitate; none of the fractions contained unchanged starting material, and all sintered with decomposition when heated to 175–180°.

When concentrated sulfuric acid was used as condensing agent, a red-brown solution was obtained which on dilution with water gave a flocculent cream-colored compound, which sintered when heated to 105°. With aqueous sodium hydroxide solutions at room temperature or below, less tar was formed than when solutions were heated. On dilution and neutralization, red viscous products were obtained. The three condensing agents have been used with hydroxy and halogenated aldehydes with formation of deeply colored products, and we have been able to characterize two which were formed from *o*-chlorobenzaldehyde as described above.

Summary

1. A simplified method of preparation and purification of 2-propionyl-1-naphthol is reported. The compound shows marked triboluminescence.

2. A method of preparation involving direct replacement of a smaller by a larger acyl group is reported.

3. Ten new derivatives have been characterized, some of which are more stable than the parent acyl and alkyl naphthols.

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[12] Hantzsch, *Ber.*, **39**, 3097 (1906).