[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NATIONAL SOUTHWEST ASSOCIATED UNIVERSITY AND THE INSTITUTE OF CHEMISTRY, NATIONAL ACADEMY OF PEIPING]

Syntheses of Compounds Related to Vitamin K. II. *p*-(3-Alkyl-4-hydroxynaphthylazo)-benzenesulfonamides

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In continuation of our work on compounds related to vitamin K[1] a number of 2-alkyl-1-naphthols have been synthesized and coupled with the diazotized sulfanilamide to yield the corresponding *p*-(3-alkyl-4-hydroxynaphthylazo)-benzenesulfonamides in which the alkyl groups are ethyl, *n*-propyl, *n*-butyl, isobutyl, *n*-amyl and *β*-phenylethyl, respectively. The parent substance, *p*-(4-hydroxynaphthylazo)-benzenesulfonamide was mentioned in the literature.[2]

All the *p*-(3-alkyl-4-hydroxynaphthylazo)-benzenesulfonamides were obtained in colored crystals except *p*-(3-isobutyl-4-hydroxynaphthylazo)-benzenesulfonamide which was a viscous mass and was difficultly purified. They possess no inhibitory effect on the growth of *Bacillus coli*, *Staphylococcus aureus* or *Streptococcus pyrogenes*.[3] The antihemorrhagic activity of these compounds and *p*-(3-methyl-4-hydroxynaphthylazo)-benzenesulfonamide will be reported later on. They behave as indicators, red in alkaline solution and yellow in acid solution.

TABLE I

2-ACYL-1-NAPHTHOLS

-1-naphthol	% yield $AlCl_3$	% yield $ZnCl_2(SnCl_4)$
2-Acetyl-	67	89
4-Acetyl-	6	0
2-Propionyl-	40	100
4-Propionyl-	4	0
2-*n*-Butyryl-	37	100
4-*n*-Butyryl-	3	0
2-Isobutyryl-	53	75
4-Isobutyryl-	34	0
2-*n*-Valeryl-	73	83
4-*n*-Valeryl-	2	0
2-*β*-Phenylacetyl-		91

Experimental

2-Alkyl-1-naphthols.—They were synthesized by Clemmensen reduction of 2-acyl-1-naphthols. Although the Stoughton method[4] of preparing 2-acyl-1-naphthols gave better result than other methods[5-9] described in the literature, the Fries rearrangement of *α*-naphthyl ester by means of aluminum chloride always gave the *p*-isomer and other by-products besides the desired 2-acyl-1-naphthol. Then the procedure was thus modified: A mixture of equal amounts of the *α*-naphthyl ester and freshly fused and powdered zinc chloride was heated on an oil-bath at 140–50° for an hour. The cold mass was treated with water to remove zinc chloride and the precipitate was recrystallized from a mixture of alcohol and acetone. The yields of 2-acyl-1-naphthols were much more satisfactory as shown in Table I. The use of anhydrous stannic chloride gave the same good results.

The 4-isobutyryl- and 4-*n*-valeryl-1-naphthols were quantitatively rearranged to the 2-isomers, respectively, by refluxing with 35% sodium hydroxide solution for two hours. However, the 4-acetyl-1-naphthol was not isomerized by the same treatment.

Among the 2-alkyl-1-naphthols prepared, the 2-*β*-phenylethyl-1-naphthol was not previously reported. It was obtained in colorless crystals from alcohol; yield, 23% and m. p. 77–78° (dec.). The reddish-orange needles of its picrate melt at 179–180 (dec.).

Anal. Calcd. for $C_{18}H_{16}O \cdot C_6H_3N_3O_7$: N, 8.81.[10] Found: N, 9.20.

p-(3-Alkyl-4-hydroxynaphthylazo)-benzenesulfonamides.—An acetic acid solution of 0.01 g. mole of 2-alkyl-1-naphthol was gradually added to a diazotized solution prepared from 0.01 g. mole of sulfanilamide. The colored precipitate was filtered and then purified either by recrystallization from a suitable solvent or by dissolving in dilute sodium hydroxide and reprecipitating with dilute hydrochloric acid. The yields and properties are listed in Table II.

TABLE II

p-(3-ALKYL-4-HYDROXYNAPHTHYLAZO)-BENZENESULFONAMIDES

Alkyl group	Solvent for recrystn.	Color[11]	Cryst. form	Yield, %	M. p., °C.	N Analyses,[11] % Calcd.	Found
Ethyl	Acetone	Yellowish-orange	Fine needles	73	249	11.83	12.13
n-Propyl	Alc.	Yellowish-orange	Fine needles	69	251	11.38	11.39
n-Butyl	Alc.	Orange-yellow	Fine needles	66	280	10.96	10.70
Isobutyl	Alc.	Dark red	Viscous mass	..	...	...	...
n-Amyl	Acetone	Yellowish-orange	Fine needles	56	260	10.57	10.04
β-Phenylethyl	NaOH + HCl	Red	Prisms	51	261	9.74	9.40

(1) Chu and Shen, *J. Chinese Chem. Soc.*, **10** (in press) (1943).

(2) Tutiva and Kawamura, *Arch. Dermatol. Syphilis*, **182**, 598 (1941).

(3) The authors are indebted to Dr. Tang Fei-Fen and his collaborators in the Central Epidemics Prevention Bureau of China for the test.

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

(5) Nencki and Sieber, *J. prakt. Chem.*, **23**, 147 (1881).

(6) Akram, Desai and Kamal, *Proc. Indian Acad Sci.*, **11A**, 139 (1940).

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

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

(9) Brewster and Watters, THIS JOURNAL, **64**, 2578 (1942).

(10) We wish to thank Dr. R. J. Williams for his generosity in permitting us to use the micro-Dumas Apparatus in the Biochemical Institute of University of Texas for some of the analyses.

(11) Compared with Mulliken's color standards.

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The Second Ionization Constant of Deuterocarbonic Acid

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Introduction.—We have measured the e. m. f. of the following cells at 25°

H_2, $KHCO_3$, K_2CO_3, KCl, AgCl, Ag (I)
D_2, $KDCO_3$, K_2CO_3, KCl, AgCl, Ag (II)