[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 AlCl₃ | % yield ZnCl₂(SnCl₄) |
|---|---|---|
| 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)