

[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 K¹ 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 -

TABLE I
2-ACYL-1-NAPHTHOLS

-1-naphthol	% yield	
	AlCl ₃	ZnCl ₂ (SnCl ₄)
2-Acetyl-	67	89
4-Acetyl-	6	0
2-Propionyl-	40	100
4-Propionyl-	4	0
2- <i>n</i> -Butyryl-	37	100
4- <i>n</i> -Butyryl-	3	0
2-Isobutyryl-	53	75
4-Isobutyryl-	34	0
2- <i>n</i> -Valeryl-	73	83
4- <i>n</i> -Valeryl-	2	0
2- β -Phenylacetyl-		91

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
<i>n</i> -Propyl	Alc.	Yellowish-orange	Fine needles	69	251	11.38	11.39
<i>n</i> -Butyl	Alc.	Orange-yellow	Fine needles	66	280	10.96	10.70
Isobutyl	Alc.	Dark red	Viscous mass
<i>n</i> -Amyl	Acetone	Yellowish-orange	Fine needles	56	260	10.57	10.04
β -Phenylethyl	NaOH + HCl	Red	Prisms	51	261	9.74	9.40

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 pyogenes*.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.

(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.

Experimental

2-Alkyl-1-naphthols.—They were synthesized by Clemmensen reduction of 2-acyl-1-naphthols. Although the Stoughton method⁴ of preparing 2-acyl-1-naphthols gave better result than other methods⁵⁻⁹ 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 C₁₈H₁₆O·C₆H₅N₂O₇: 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.

(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.

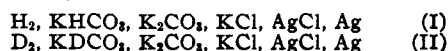
(11) Compared with Mulliken's color standards.

KUNMING, YUNNAN, CHINA RECEIVED JANUARY 22, 1944

The Second Ionization Constant of Deuterocarbonic Acid

BY JAMES CURRY AND Z. ZIMMERMAN HUGUS, JR.

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



The potential of cell I is given by

$$E = E_0 - \frac{RT}{F} \ln m_{\text{H}} m_{\text{Cl}} - \frac{RT}{F} \ln f_{\text{H}} f_{\text{Cl}} \quad (1)$$

where E_0 is the standard electrode potential of the silver-silver chloride electrode in water referred to hydrogen, m is the concentration in molal terms and f is, the activity coefficient of the quantities indicated by the subscripts.

The second thermodynamic ionization constant for proto-carbonic acid is

$$K_{\text{H}} = \frac{m_{\text{H}} m_{\text{CO}_2} f_{\text{H}} f_{\text{CO}_2}}{m_{\text{HCO}_3} f_{\text{HCO}_3}} \quad (2)$$

Replacing m_{H} in (1) by its value from (2) and solving for the negative logarithm of the ionization constant we obtain

$$pK_{\text{H}} = \frac{E - E_0}{0.0591} + \log \frac{m_{\text{HCO}_3} m_{\text{Cl}}}{m_{\text{CO}_2}} + \log \frac{f_{\text{HCO}_3} f_{\text{Cl}}}{f_{\text{CO}_2}} \quad (3)$$

If we define pK_{H} as the sum of the first two terms on the right-hand side of (3) we then get

$$pK_{\text{H}} = pK_{\text{H}}^* + \log \frac{f_{\text{HCO}_3} f_{\text{Cl}}}{f_{\text{CO}_2}} \quad (4)$$

The analogous equations for cell II are

$$pK_{\text{D}} = \frac{E - E'_0}{0.0591} + \log \frac{m'_{\text{DCO}_3} m'_{\text{Cl}}}{m'_{\text{CO}_2}} + \log \frac{f'_{\text{DCO}_3} f'_{\text{Cl}}}{f'_{\text{CO}_2}} \quad (5)$$

$$pK_{\text{D}} = pK_{\text{D}}^* + \log \frac{f'_{\text{DCO}_3} f'_{\text{Cl}}}{f'_{\text{CO}_2}} \quad (6)$$

where K_{D} is the second ionization constant of deuterio-carbonic acid and the primes refer to the values for D_2O . E'_0 includes the standard electrode potential of the deuterium electrode and the silver-silver chloride electrode in D_2O .

Experimental.—The purification of the salts and deuterium oxide, the preparation of the silver-silver chloride electrode, the cell and the potentiometer have been described previously.¹ A detailed description of the hydrogen (deuterium) electrode will be given in another article. In order to avoid loss of carbon dioxide and consequent change in the carbonate-bicarbonate concentrations a device was developed which circulated the hydrogen in a closed system. This also allowed the use of macro quantities of deuterium but at the same time avoided the necessity of using a large quantity of this gas.

This device consisted of a short endless system of tubing which was fastened to the end of the cell containing the hydrogen electrode. One portion of the system was enlarged and contained a Bunsen valve. The pressure in part of the system could be increased by raising a column of mercury. This caused the hydrogen to bubble through the solution around the platinum electrode. The mercury was then lowered and the cycle repeated. A motor and eccentric raised and lowered the mercury column at a rate of fifteen times per minute. The electrode itself was spiral in shape and was platinized in a conventional manner.

The hydrogen was obtained from a commercial tank and was purified by passing it through alkaline pyrogallol, sulfuric acid and distilled water. The deuterium was prepared by electrolyzing 98.9% D_2O . For one determination about 100 cc. of deuterium was used. The circulation system, including the cell, had a volume of 35 cc. and the excess gas was used for flushing purposes.

Constant readings were obtained with no great difficulty, the e. m. f. of the cell usually varied no more than 0.1 mv. over a period of an hour or two. Before measurements were made on cells (I) and (II) the reliability of the

circulating device was tested on the cell H_2 , HCl , AgCl , Ag . These measurements were found to be quite satisfactory.

Results.—The results obtained are summarized in the following table.

$E_0 = 0.2224$		$E'_0 = 0.2190$		E	pK^*
KCl	bicarbonate	Molality K_2CO_3	$X \times 10^4$		
H_2O					
0.01356	0.01572	0.01234	1.7	0.9263	10.158
.02841	.02976	.03055	2.4	.9129	10.133
98.9% D_2O					
.01111	.01286	.01169	1.2	.9663	10.740
.02444	.02883	.02887	1.5	.9468	10.707

$$K_{\text{H}}/K_{\text{D}} = 3.95$$

Discussion.—The fourth column gives the amount of potassium carbonate hydrolyzed. This was calculated according to the method of MacInnes and Belcher² and was taken into account in calculating pK^* . The value of K_w for D_2O was taken as 0.16×10^{-14} . As is customary, the values of E have been corrected to a hydrogen (deuterium) pressure of one atmosphere.

The values obtained for pK_{H}^* agree well with those of MacInnes and Belcher at similar ionic strengths. The first agrees within 0.04%; the second within 0.3%.

E'_0 is made up of the standard electrode potential of the silver-silver chloride electrode in D_2O and the deuterium ion-deuterium electrode. As in previous work¹ the standard electrode potential for the silver-silver chloride electrode was taken to be the same in D_2O as in H_2O . For the deuterium electrode the value obtained by Abel, Bratu and Redlich,³ namely, 0.0034 volt, was used. These authors used a micro method to measure this value and it had been our original intention to redetermine it using our macro method but events precluded this.

In a comparative method, such as the present one, the quantity desired is $K_{\text{H}}/K_{\text{D}}$. This can be obtained through a knowledge of the ratio $pK_{\text{H}}/pK_{\text{D}}$ and the value of K_{H} . Because the solutions used were quite dilute a close approximation to this latter ratio can be obtained by finding $pK_{\text{H}}^*/pK_{\text{D}}^*$, the numerator and denominator being taken at the same ionic strengths. The reason for this is that the logarithmic term of the ratio of activities in both (4) and (6) is small compared to pK^* .

Using the values of pK_{D}^* in the table and finding pK_{H}^* for the same ionic strengths from the work of MacInnes and Belcher, we calculate from the first measurement in D_2O that $pK_{\text{H}}^*/pK_{\text{D}}^*$ is equal to 0.94590 and from the second a value of 0.94415. Thus, for the reasons given above, we can take the average of these to be equal to $pK_{\text{H}}/pK_{\text{D}}$. Using this average and MacInnes and Belcher's value of K_{H} , namely, 5.61×10^{-11} ,

(2) MacInnes and Belcher, *ibid.*, **55**, 2630 (1933).

(3) Abel, Bratu and Redlich, *Z. physik. Chem.*, **A173**, 353 (1935).

(1) Curry and Hazelton, *This Journal*, **60**, 2773 (1938).

the second ionization constant for deuterio-carbonic acid may be calculated to be 1.42×10^{-11} . Thus K_H/K_D is equal to 3.95.

It should be pointed out that this value of K_H/K_D for the second ionization constant of carbonic acid agrees within 4% of that predicted by the curve of Rule and LaMer⁴ and confirmed by Martin and Butler.⁵

(4) Rule and LaMer, *THIS JOURNAL*, **60**, 1974 (1938).

(5) Martin and Butler, *J. Chem. Soc.*, 1366 (1939).

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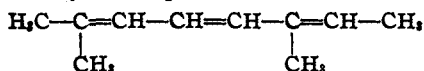
WILLIAMSTOWN, MASS.

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The Production of α - and β -Pyronene from *allo*-Ocimene

BY L. A. GOLDBLATT AND S. PALKIN¹

Among the products obtained in the pyrolysis of α -pinene in the vapor phase,^{2,3,4} at about 375°, the acyclic terpene



(2,6-dimethyl-2,4,6-octatriene) is of the greatest interest, both from a practical and theoretical point of view. The simultaneous formation of the monocyclic hydrocarbons α - and β -pyronene was first observed by Dupont and Dulou, who postulated³ that they were obtained from α -pinene by a simultaneous and independent reaction, namely, rupture of the four-membered ring in α -pinene, and not by further isomerization of either *allo*-ocimene or dipentene, other products of the pyrolysis. They later reported⁵ that this hypothesis had been confirmed.

In the course of the work of the Naval Stores Research Division on the vapor phase thermal isomerization of terpene hydrocarbons, it was found that the pyronenes are in fact obtained by the recyclization of *allo*-ocimene.⁶

The apparatus used for the pyrolysis is shown in Fig. 1. This consists essentially of a pyrolysis tube, together with a suitable condensing and receiving system. Heat for the pyrolysis tube is supplied by means of a bath of "HTS" (a commercial mixture of sodium and potassium nitrate and nitrite). This in turn is heated by passage of

(1) Died May 2, 1943.

(2) Arbuzov, *J. Gen. Chem. (U. S. S. R.)*, **3**, 21 (1933); *Ber.*, **67B**, 563 (1934).

(3) Dupont and Dulou, *Compt. rend.*, **201**, 219 (1935).

(4) Goldblatt and Palkin, *THIS JOURNAL*, **63**, 3517 (1941).

(5) Dupont and Dulou, *Atti. X° Congr. Intern. Chim.*, **3**, 127 (1939).

(6) Work of the Naval Stores Research Division on the vapor phase cyclization of *allo*-ocimene has been temporarily discontinued owing to preoccupation with problems more closely related to the war effort. Reporting of these preliminary results at this time is prompted by a communication from Dr. J. E. Hawkins and R. E. Fuguitt of the University of Florida, who have confirmed this observation from information obtained in the study of the thermal isomerization of α -pinene in the liquid phase, and who have generously undertaken to remove any question as to priority of this discovery in a forthcoming publication.

an electric current through 25 feet (resistance, 16 ohms) of no. 20 Nichrome wire wound on asbestos-paper covering a suitable length of ordinary 1.5-inch iron pipe. Temperature was controlled by a variable voltage transformer and measured by a movable thermocouple in a glass well placed vertically in the center of the reaction tube. In normal operation the temperature generally did not vary more than 5° for about half the length of the pyrolysis tube, although the temperature was materially lower at both ends. *allo*-Ocimene was supplied to the pyrolysis tube by a Tropsch and Mattox pump⁷ capable of supplying *allo*-ocimene at a definite rate varying from about 50 to 750 cc. per hour with a precision of 1%. Flow of *allo*-ocimene supplied by the pump was made more uniform by inserting a coil of glass tape just inside the spherical joint.

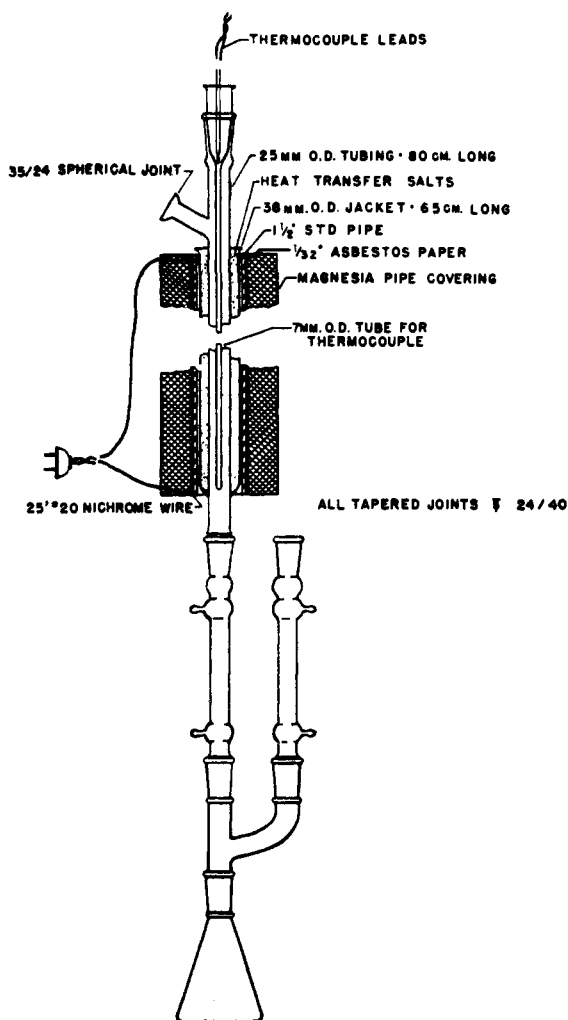


Fig. 1.—Pyrolysis unit.

Change in refractive index provides a convenient guide to the extent of isomerization. A sample of *allo*-ocimene having the characteristics

(7) Tropsch and Mattox, *Ind. Eng. Chem.*, **26**, 1338 (1934).