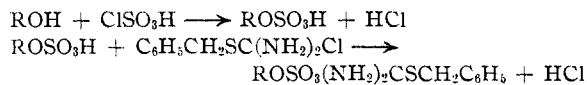


NOTES

Identification of Alcohols and Alkyl Hydrogen Sulfates with S-Benzylthiuronium Chloride

BY ROBERT K. BAIR AND C. M. SUTER

The sodium salts of many acids including sulfonic acids¹ react with S-benzylthiuronium chloride to form derivatives which are of value in the identification of the original materials. The reagent is produced in nearly quantitative yield by the action of benzyl chloride with thiourea.^{1,2} It has now been found that most alcohols are easily identified by this same reagent through first converting them to the corresponding alkyl hydrogen sulfates by warming in dioxane solution with chlorosulfonic acid. The benzylthiuronium salts of



methyl and ethyl hydrogen sulfate are too soluble in water to be isolated readily and the *n*-octyl compound showed an anomalous melting point

TABLE I
S-BENZYLTHIURONIUM DERIVATIVES

Alcohol	M. p., °C. (cor.)	Nitrogen, %	
		Calcd.	Found
<i>n</i> -Propyl	111.5-112.5	9.15	9.16
<i>i</i> -Propyl	142-143	9.15	9.07
<i>n</i> -Butyl	100-101	8.75	8.83
<i>s</i> -Butyl	117-119	8.75	8.73
<i>i</i> -Butyl	136-137	8.75	8.91
<i>n</i> -Amyl	85-86 ^e	8.38	8.25
<i>n</i> -Hexyl	85-86 ^e	8.04	7.87
<i>n</i> -Heptyl	77-79	7.74	7.33
<i>n</i> -Octyl	42-70	7.45	7.91
<i>n</i> -Decyl	73-75 ^a	6.98	6.88
Lauryl ^b	74-76	6.48	6.55
Myristyl ^b	87-88	6.08	6.02
Cyclohexyl ^{c,d}	163-164	8.10	8.05
Bornyl ^e	174-175	7.01	7.12
Menthyl ^e	149-150	6.98	6.97
Ethylene glycol	180-181	10.10	10.39

^a Nitrogen analyses by Dr. T. S. Ma, University of Chicago.

^b Chlorosulfonic acid added to solid alcohols dissolved in dioxane.

^c Thiuronium derivatives made from alkyl hydrogen sulfates.

^d We are indebted to Dr. Sydney Archer for purifying samples of the last four compounds.

^e Mixed melting points were taken: *n*-amyl and *n*-hexyl, 77-82°; *n*-heptyl and *n*-decyl, 53-71°.

behavior although the analysis was satisfactory. Ethylene glycol was identified as the bis-(hydrogen sulfate) but the behavior of other glycols was not studied.

Obviously this method of identification is applicable to sodium alkyl sulfates as such and this is of considerable interest because of the varied commercial uses of these compounds. However, the difference in melting point for the decyl and lauryl compounds is small.

Procedure.—About 5 drops of the alcohol is added to a mixture of 4 drops of chlorosulfonic acid and 5 drops of dioxane. If hydrogen chloride is not immediately evolved, the resulting mixture is warmed with shaking and allowed to stand for five or ten minutes. Then after the addition of 1 ml. of water, 1 ml. of a saturated aqueous solution (or 15% alcohol solution) of S-benzylthiuronium chloride is added. If crystals do not form in a few minutes the solution is chilled in an ice-bath. The derivatives of the lower molecular weight alcohols (to *n*-hexyl inclusive) can be recrystallized from 10% ethyl alcohol, and derivatives of higher alcohols from 50% alcohol. In preparing samples for analyses the quantities used in this procedure were multiplied by five.

The corresponding *p*-chlorobenzylthiuronium derivatives were also made from about eight alcohols; however, several of these were waxy, difficult to filter and to obtain in a pure state. Also five of them melted between 80 and 90°. No derivatives of methanol and ethanol were obtained by using either the *p*-chloro-S-benzyl- or S-benzylthiuronium chloride.

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RECEIVED MAY 22, 1942

The Dehydration of 1,5-Hexadiene-3-ol to 1,3,5-Hexatriene and 1,3-Cyclohexadiene¹

BY LEWIS W. BUTZ

That the dehydration of 1,5-hexadiene-3-ol under the conditions recently described² yields about 70% of 1,3,5-hexatriene was demonstrated by conversion of part of the products to 1-vinylanthraquinone. At the same time it appeared that 1,3-cyclohexadiene was formed in about 30% yield, since reaction of the hydrocarbon products with 1,4-naphthoquinone gave a 1,4-ethano adduct. The alternative explanation would be that hexatriene is converted to cyclohexadiene when

(1) Chambers and Watt, *J. Org. Chem.*, **6**, 376 (1941).

(2) Donleavy, *THIS JOURNAL*, **58**, 1004 (1936).

(1) Not subject to copyright.

(2) I. Butz, E. Butz and Gaddis, *J. Org. Chem.*, **5**, 178 (1940).

heated with naphthoquinone at 50°, a result hardly to be expected.

In contact with maleic anhydride at 30°, the hydrocarbon products gave a crystalline compound which was different from the adduct obtained by Farmer and Warren³ from hexatriene and maleic anhydride at 100°. Since Farmer and Warren considered their compound to be an ethylenetetrahydrophthalic anhydride, it appeared likely that the new isomer was the vinyltetrahydrophthalic anhydride, the normal adduct, and this view was expressed publicly.⁴

This has now been shown not to be the case. The substance, m. p. 147°, does not depress the m. p. of the ethanotetrahydrophthalic anhydride prepared⁵ from cyclohexadiene and maleic anhydride. This is further evidence that the hydrocarbon obtained by the dehydration of the hexadienol contained cyclohexadiene. While the possibility of a direct hexatriene → cyclohexadiene transformation is still not excluded, it must be supposed that it occurs, if at all, during the dehydration of the hexadienol rather than during the reaction with naphthoquinone or maleic anhydride at 50 or 30°. However, it appears that the hexatriene prepared by this method is not always contaminated with so much cyclohexadiene, and the formation of the latter must depend on small variations in procedure, because the hydrocarbon has been found⁶ not to yield, upon reaction with 5-acetoxy-1,4-toluquinone, any of the adducts obtained from cyclohexadiene and this quinone.

(3) Farmer and Warren, *J. Chem. Soc.*, 897 (1929).

(4) *J. Wash. Acad. Sci.*, 29, 548 (1939).

(5) I. G. Farbenindustrie A.-G., *Chem. Zentr.*, 100, II, 2502 (1929).

(6) E. Butz and L. Butz, *J. Org. Chem.*, 7, 199 (1942).

BUREAU OF ANIMAL INDUSTRY
U. S. DEPARTMENT OF AGRICULTURE
BELTSVILLE, MARYLAND RECEIVED JUNE 13, 1942

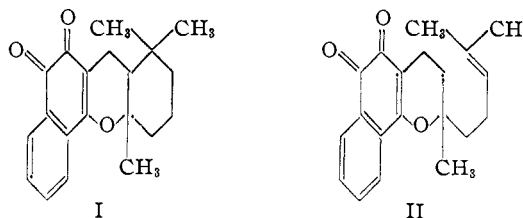
The Condensation of β -Cyclogeraniol with Leucoisonaphthazarin

BY MARSHALL D. GATES AND FERNANDA MISANI

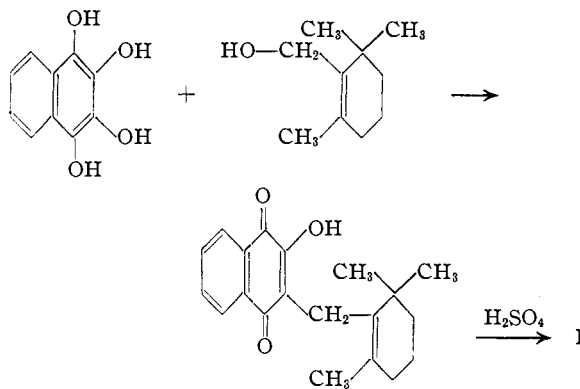
In a recent paper Fieser and Gates¹ described the preparation of β -geranolapachone, a member of the β -lapachone series, by cyclization of 2-hydroxy-3-geranyl-1,4-naphthoquinone with concentrated sulfuric acid. The high melting point of this compound (234°) suggests that further cyclization of the side chain may have taken

(1) Fieser and Gates, *THIS JOURNAL*, 63, 2948 (1941).

place to give structure I rather than the supposed structure II.



A choice between these two structures was readily made by synthesizing structure I by application of the general scheme employed by Fieser and Gates.¹



The β -cyclogeraniol employed (m. p. 44°) was prepared by Meerwein-Ponndorf reduction of β -cyclocitral according to Kuhn and Hoffer.² Condensation with leucoisonaphthazarin gave the desired 2-hydroxy-3-(β -cyclogeranyl)-1,4-naphthoquinone in rather poor yield, but in easily isolated form. On cyclization with sulfuric acid, β -cyclogeranolapachone (I) was obtained. It proved to be identical with β -geranolapachone prepared according to Fieser and Gates, and their β -geranolapachone must therefore be regarded as β -cyclogeranolapachone (I).

The conditions used in the condensation of allylic alcohols with hydroxyhydroquinones in these syntheses are not sufficiently acidic (oxalic acid) to bring about cyclization of the geranyl group during the condensation. This is shown by the non-identity of the products obtained by the condensation of geraniol and β -cyclogeraniol with leucoisonaphthazarin.

Experimental Part³

Isonaphthazarin.—The following procedure represents an improvement over that reported by Fieser and Gates.¹ A solution of 8.9 g. of 2-hydroxy-1,4-naphthoquinone

(2) Kuhn and Hoffer, *Ber.*, 67, 357 (1934).

(3) All melting points are corrected.

(purified through the methoxy compound) in 500 cc. of water containing 4.3 g. of sodium bicarbonate was treated with 20 cc. of 30% hydrogen peroxide (superoxol). The solution rapidly darkened and, after standing for thirty-four hours, a crop of dull red large leaves had separated, 3.2 g. (43% based on 2-hydroxy-1,4-naphthoquinone utilized). One crystallization from dioxane gave pure isonaphthazarin. Acidification of the aqueous filtrate yielded 2.1 g. of orange precipitate which consisted of unchanged 2-hydroxy-1,4-naphthoquinone plus a small amount of isonaphthazarin. On several occasions, use of less pure 2-hydroxy-1,4-naphthoquinone as starting material led to much lower yields.

2-Hydroxy-3-(β -cyclogeranyl)-1,4-naphthoquinone.

Isonaphthazarin (2.0 g.) was reduced as described by Fieser and Gates¹ and the leuco compound heated in the dark under nitrogen for forty-eight hours at 65-70° with 1.0 g. of β -cyclogeraniol² (m. p. 44°), 0.6 g. of anhydrous oxalic acid and 20 cc. of dioxane. The processing of the reaction mixture included the following steps: extraction of the unchanged leucoisonaphthazarin with aqueous hydrosulfite, reduction with concentrated aqueous hydrosulfite, and extraction from ether-petroleum ether with Claisen's alkali. The crude phenolic portion thus obtained was chromatographed after air oxidation on freshly ignited magnesium sulfate. On development with petroleum ether, a weakly adsorbed bright yellow band readily passed into the filtrate. Similar filtrates from systematic reabsorptions of the column eluate were combined and on concentration to dryness under reduced pressure afforded 99 mg. of solid residue which after three crystallizations from ether-petroleum ether gave 36 mg. of golden yellow rectangular plates, m. p. 135-135.5°. It is quite soluble in the ordinary organic solvents, fairly soluble in warm petroleum ether, much less soluble cold, and dissolves in dilute alcoholic alkali to give the beautiful scarlet characteristic of alkali salts of 2-hydroxy-1,4-naphthoquinones. It dissolves in concentrated sulfuric acid to give a deep orange-red solution. Two further crystallizations to obtain a sample for analysis did not alter the melting point.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 77.38; H, 7.15. Found: C, 77.50; H, 7.23.

β -Cyclogeranolapachone (I).—A solution of 11 mg. of 2-hydroxy-3-(β -cyclogeranyl)-1,4-naphthoquinone in ice-cold concentrated sulfuric acid (0.3 cc.) was allowed to stand several minutes, then diluted with ice water. The precipitated dark orange-brown material was taken into ether, washed with water, bicarbonate and brine, and concentrated to dryness. The residue was taken into benzene-hexane and chromatographed on freshly ignited magnesium sulfate. Development with 50% benzene-hexane left a broad salmon-pink band in the middle of the column which was sectioned out and eluted with ether. After evaporation of the ether, the solid residue was crystallized twice from pure acetone to give 3.5 mg. of orange-red prismatic blades, m. p. 232-233.3°. A mixed melting point with β -geranolapachone prepared according to Fieser and Gates¹ showed no depression.

DEPARTMENT OF CHEMISTRY
BRYN MAWR COLLEGE
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RECEIVED MAY 29, 1942

Riboflavin Estimation in Fruits and Vegetables

BY G. MACKINNEY AND J. M. SUGIHARA

As part of a collaborative project,¹ it was recently necessary to make a series of chemical determinations of thiamin and riboflavin in certain fruits and vegetables, and the Conner-Straub procedure² was followed. Unfortunately, at the beginning, Supersorb,³ the specific adsorbent for riboflavin was unavailable. An empirical method was, therefore, evolved, and we hoped, later, to correlate results into the series by concurrent assays on additional samples on arrival of the adsorbent. This comparison may now be made and, subject to certain provisos, we believe the modification accurately reflects differences in riboflavin content within a series. With respect to absolute values, it is in accord with microbiological assay by means of *Lactobacillus casei*. It has, further, certain advantages: increased light stability, no adsorbent is needed and the riboflavin in the aqueous buffer exhibits approximately twice the fluorescence found in pyridine-acetic solution, with consequent decrease in the percentage reading error.

The Conner-Straub procedure is followed in detail in extraction and preparation of the sample, except that, in the case of fruits, 10 ml. of pectinol (1 g. in 25 ml.) is added per 50-ml. of sample, in addition to the clarase. The whole is then incubated at 45° for two hours. The pectinol is absolutely necessary for prunes, apricots, dates, etc., to produce a satisfactory solution. A 10-20 ml. aliquot is then heated to boiling with 5 ml. of 2% acetic, as in (1), made to volume, 50 ml., with buffer, and a 15-ml. aliquot treated for a minimum of three minutes with 1 ml. of potassium permanganate, and decolorized with 3 ml. of 3% hydrogen peroxide. The solution is then filtered and compared with buffered standards at pH 6.0 in a Coleman fluorophotometer. The B₂ filter for the exciting light (Hg arc) cuts out completely above 4900 Å. and for the fluorescent light, below 5100 Å. The cut-out is sharp, and, for the latter filter, the transmission rises from zero at 5100 to over 90% at 5400 Å. Quinine sulfate and thiochrome have no effect on the galvanometer with these filters, at least in the concentrations used. In the majority of plant extracts treated as above, there appear to be no other water-soluble fluorescent compounds in sufficient quantities to interfere, though trouble might be anticipated in those botanical families where anthraquinone glucosides occur. However, since we do not know the behavior of these compounds on Decalso or Supersorb, similar difficulties might arise with either method.

(1) With the Department of Home Economics.

(2) Conner and Straub, *Ind. Eng. Chem., Anal. Ed.*, **13**, 385 (1941).

(3) Supersorb, Florisil or Floridin is a Fuller's Earth; Decalso, a synthetic zeolite, obtainable through supply houses, Clarase (Takamine Laboratories, N. Y.) and Pectinol (Rohm and Haas, Philadelphia) are commercial enzyme preparations.

TABLE I
RIBOFLAVIN ESTIMATES IN FRUITS AND VEGETABLES^a IN MICROGRAMS PER GRAM

Material	Aqueous buffer, no adsorption	20 hours later	Pyridine-acetic adsorbed	20 hours later	Microbiological ^b	Thiamin, μg./g.
Asparagus, fresh	1.15	1.00	1.13	0.45		2.19
Asparagus, blanched	1.25		1.18			2.60
Broccoli, fresh	...		0.79			0.77
Broccoli, dehydrated	6.28		4.30			3.71
Broccoli, dehydrated	8.66		7.16			3.97
Broccoli, dehydrated	13.0		13.4		12.6	7.25
Peas, fresh	0.86	0.65	0.67	.22	1.5	1.16
Peas, fresh	.80		.72			0.91
Peas, cooked	.83	0.63	.78	.33		1.00
Peas, dehydrated	4.01		5.73		5.5	4.38
Peas, dehydrated	3.36		4.78			4.16
Spinach, dehydrated	23.4		18.6		23.7	10.2
Rice bran, concd.	7.74	6.85	5.44	2.71		141.0
Apricots, dried, sulfured	1.94	1.94	1.63	0.51		0.21
Prunes, dried	1.59	1.64	1.27	.20		1.24
Dates, Deglet Noors	1.14		0.30			0.53
Dates, Deglet Noors	0.73	0.77	0.40	.05		0.52
Grass, dehydrated	8.23	7.80	11.5	4.78		5.28

^a It should be understood that the estimates on the materials assayed are valid only for these samples, purchased for the most part on the local market, without consideration of variety, maturity or possible abnormal local conditions caused by climate, Jan.-March, 1942. ^b We thank Miss M. B. Smith of the Department of Home Economics for these values.

Riboflavin estimates are given, Table I, in column 2 by the above procedure, and in column 4 after passage over Decalco and Supersorb, where the Conner-Straub procedure for both B₁ and B₂ is followed. The same samples measured twenty hours later, columns 3 and 5, after standing in the laboratory away from direct lighting, clearly show the higher light stability of our extract. We are greatly indebted to Professor Agnes Fay Morgan for permission to include, in column 6, certain microbiological assays on the same samples with *Lactobacillus casei*. They indicate very satisfactory agreement with the chemical method over the range 1 to 20 μg. per gram of sample. We include thiamin values in column 7. The rice bran concentrate, a trade product, is of interest because the thiamin value is approximately 10% higher than the minimum stated on the label, the riboflavin roughly 8 or 35% lower, depending upon whether we take the value of column 2 or 4. The thiamin content of the sulfured apricot is low, as might have been predicted.

With two reproducible exceptions, grass and peas after dehydration, our simpler procedure yields consistently higher results. In the case of the dehydrated peas there is definitely interference, possibly from a compound which forms a discrete yellow zone on the Supersorb, not found in the fresh peas, removed with the riboflavin by the eluting solvent. The values listed in Table I for a given vegetable are from different samples, variously treated. In general, at levels of 20 μg. per g., the results are reproducible within 5-10%, and 5-20% at 1.0 μg. per g.

The effect of diffuse light on the standards is shown in Table II. The concentration used at zero time is approximately 0.1 μg. per ml.

Our simpler procedure is certainly worth consideration where the adsorbent is unavailable, be-

TABLE II
EFFECT OF LIGHT ON PERCENTAGE RETENTION OF RIBOFLAVIN IN STANDARDS

Time in hours	0	3	6	24
Pyridine-acetic	100	81.1	64.9	32.4
Buffer, pH 6.0	100	91.5	88.1	76.3

cause comparative variations are reflected with accuracy in the figures. It is necessary to be more cautious in considering absolute values. Discussing specifically the vitamin A potency of foods, Booth⁴ suggests that physiological responses should be expressed in International Units, and that only chemical results should be based on the gram and the liter. We may also note that it does not follow *a priori* that either of the above procedures has been absolutely (as distinct from comparatively) calibrated against *Lactobacillus* or any other bio-assay. In other words, the true chemical concentration may not represent the real biological potency. This may be illustrated in the case of carrots and spinach, where the former may have 2 to 4 times the carotene content, but where there is still doubt concerning the relative biological potencies, in terms of vitamin A bio-assay.

DIVISION OF FRUIT PRODUCTS
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RECEIVED MAY 4, 1942

(4) Booth, *Food Manuf.*, 17, 60 (1942).

The Dipole Moments of Cyclohexanol and Cyclohexanone in Dioxane

By I. F. HALVERSTADT¹ AND W. D. KUMLER

In the course of an investigation on the structure of the bile acids it was desirable to know the dipole moments of cyclohexanol and cyclohexanone in dioxane. These compounds have been measured in benzene by Williams,² the moments being cyclohexanol, 1.9, and cyclohexanone 2.9.³

$$P_{E_2} = p_{20} M_2$$

$$\mu = 0.0127 \sqrt{(P_{E_2} - P_{E_1})T}$$

P_{E_2} values were calculated from the molar refractivities of the electron groups present in the molecules.

The $\epsilon_{12}-\omega_2$ curves were linear for both compounds and the extrapolated value of ϵ_1 was approximately equal to the observed value, indicating that the compounds are not associated in these solutions.

TABLE I
MEASUREMENTS IN DIOXANE AT 25°

Cyclohexanol			Cyclohexanone							
ω_2	η_{12}	ϵ_{12}	ω_2	η_{12}	ϵ_{12}	α	β	P_{E_2}	P_{E_1}	μ
0.002696	0.97424	2.2237	0.002580	0.97422	2.2395					
.005279	.97447	2.2337	.004785	.97448	2.2631					
.007566	.97476	2.2432	.008013	.97472	2.2972					
.010630	.97508	2.2554	.009462	.97491	2.3128					
.012633	.97524	2.2639	.011496	.97512	2.3342					
.014741	.97549	2.2723	.014441	.97546	2.3657					
	ϵ_1 measured	ϵ_1 extrapolated	η_1 extrapolated							
Cyclohexanol	2.2123	2.2126	0.97395			4.05	0.104	97.8	29.2	1.82
Cyclohexanone	2.2128	2.2121	0.97395			10.63	0.102	202.2	27.7	2.90

The symbols in the equations and tables are the same as those given previously.⁴ The equations used in calculating the moments are⁴

$$p_{20} = \frac{3\alpha\epsilon_1}{(\epsilon_1 + 2)^2} + (\tau_1 + \beta) \frac{(\epsilon_1 - 1)}{(\epsilon_1 + 2)}$$

(1) Abraham Rosenberg Fellow in Pharmaceutical Chemistry 1941-1942.

(2) Williams, THIS JOURNAL, **52**, 1831 (1930).

(3) Through a typographical error, the moment of cyclohexanone is listed in William's article as 2.8.

(4) Halverstadt and Kumler, "A Critical Study of Dielectric Polarization Concentration Curves," in publication.

Eastman Kodak Co. practical cyclohexanol was dried over "Drierite" and twice fractionally distilled through a Widmer column, b. p. 160.9-161.3° cor. at 759 mm.

Eastman Kodak Co. practical cyclohexanone was twice fractionally distilled through a Widmer column, b. p. 157.0-157.5° cor. at 759 mm.

COLLEGE OF PHARMACY,
UNIVERSITY OF CALIFORNIA
SAN FRANCISCO, CALIFORNIA

RECEIVED MAY 5, 1942

NEW BOOKS

The Tools of the Chemist. Their Ancestry and American Evolution. By ERNEST CHILD. Reinhold Publishing Corporation, New York, N. Y., 1940. 220 pp. Price, \$3.50.

"Tools of the Chemist," by Ernest Child is an historical account of the development of laboratory apparatus and ware with special emphasis on American enterprise. The book is divided into three parts. Part I, "People and Events in American Chemistry," is entirely historical and biographical and reviews the accomplishments of the pioneers of our science in this country. This part of the book is particularly valuable to the student of the history of chemistry and makes interesting and fascinating reading.

The major portion of the book, Part II, describes the "Ancestry and Development of American Chemical Laboratory Apparatus." In turn, the following appliances, ware and other materials are taken up: balances, glass, porcelain and silica ware, filter paper, heating apparatus, metal laboratory ware, platinum, alundum, rubber ware and optical apparatus. The section on balances is by far the best presented and is given in greatest detail, the illustrations being particularly well chosen to show the earlier forms. One is forcibly reminded throughout the reading of this section of the important and vital role the American chemist has had in developing and perfecting our modern chemical tools. More illustrations of present types of apparatus would have added interest to the book.