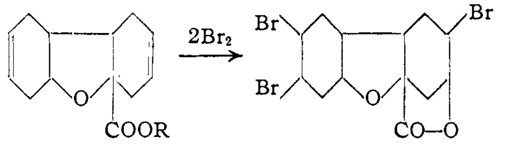
imino-ether formation involving the resulting hydroxy nitrile ester has not been demonstrated. We observed, however, that the saturated compound, 2,2-diethylvaleronitrile (obtained by hydrogenation of 2,2-diethyl-4-pentenenitrile over Pd:$CaCO_3$, b.p. 84–86° (20 mm.)), when subjected to the same experimental conditions was recovered largely unchanged; only a small amount of the amide[7] (crystallized from petroleum ether, m.p. 68–69.5°) was formed.

Craig[3] demonstrated that similar cyclizations of α-disubstituted allylacetic acids or esters could be carried out by the use of bromine. We became aware of this possibility during a study of the reactions of 2,3,4,5-bis-(Δ^2-butenylene)-tetrahydrofuroic acid (IV)[8] (octahydrodibenzofuran-4a-carboxylic acid). When either the acid or its methyl ester was treated with an excess of bromine in chloroform at 0°, there was obtained a neutral, colorless crystalline product (needles from acetic acid, m.p. and mixed m.p. 228–230° dec.) which contained but three atoms of bromine. *Anal.* Calcd. for $C_{13}H_{15}O_3Br_3$: Br, 52.2. Found: Br, 51.8, 52.2. This we believed to be the tribromolactone (V).



IV V

R = H. CH_3–

More detailed study of the mechanism of the transformations involving allylic systems of this type may be expected to contribute to the knowledge of the structure of the compounds related to IV and V. It has been pointed out that such a study has been undertaken in another laboratory.[9]

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[7] C. L. Carter and S. N. Slater, *J. Chem. Soc.*, 130 (1946).

[8] This structure was proposed by J. C. Hillyer, *et al.*, *Ind. Eng. Chem.*, **40**, 2216 (1948). An extensive series of compounds may be derived from the aldehyde formed by condensation of furfural with butadiene. We do not regard this structure as unequivocally established.

[9] See Craig, ref. 3, footnote 6.

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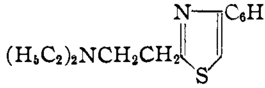
β,β'-Di-(2-thiazolyl)-diethyl Sulfides

BY EDGAR A. STECK AND LYNN T. FLETCHER

RECEIVED APRIL 29, 1952

A recent publication of Dahlbom[1] prompts us to record observations of similar nature in attempts to prepare 2-(β-diethylaminoethyl)-4-phenylthiazole (I). It was found that the action of hydrogen sulfide on β-diethylaminopropionitrile had not produced the expected thioamide (II), but, rather, another substance, since (I) did not result from the reaction of the intermediate with phenacyl bromide. The intermediate, which we did not obtain in crystalline form, was indicated to be β,β'-thiodi-(propionthioamide) (III) through analyses of the compounds (IV) and (V) formed by reaction with phenacyl bromide and chloroacetone. Only the β,β'-di-(4-substituted-2-thiazolyl)-diethyl sulfide type could be isolated, and no further study was done. Dahlbom[1] has given the problem more detailed consideration.



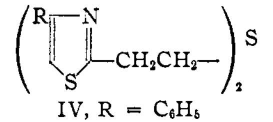
I

$(H_5C_2)_2NCH_2CH_2CSNH_2$

II

$S(CH_2CH_2CSNH_2)_2$

III



IV, R = C_6H_5
V, R = CH_3

Experimental

β,β'-Thiodi-(propionthioamide) (III).—A mixture of 139.0 g. (4.1 moles) of hydrogen sulfide, 180.9 g. (1.43 moles) of β-diethylaminopropionitrile and 700 cc. of absolute ethanol was shaken at 60° for 10 hours. The viscous, brownish residue which remained after removal of the low-boiling material weighed 150.0 g. (50.5% yield). Attempts to induce the thioamide to crystallize were unsuccessful.

β,β'-Di-(4-phenyl-2-thiazolyl)-diethyl Sulfide (IV).—A solution of 17.5 g. (0.08 mole) of crude (III) in 175 cc. of absolute ethanol was treated with 20.0 g. (0.1 mole) of phenacyl bromide and refluxed three hours. The cooled mixture gave a greenish-white solid (21.3 g., m.p. 192–193°) when a large volume of ether was added. The crude dihydrobromide was converted to the base (IV) with aqueous ammonia. After three crystallizations from hexane, 8.7 g. (43%) of pure (IV) resulted; m.p. 68.2–69.2° cor. (lit.[1] m.p. 68–69°).

Anal. Calcd. for $C_{22}H_{20}N_2S_3$: N, 6.86; S, 23.54: mol. wt., 408.6. Found:[2] N, 6.98; S, 23.48, 23.62; mol. wt., 420.

β,β'-Di-(4-methyl-2-thiazolyl)-diethyl Sulfide (V).—The reaction of 0.08 mole of crude (III) with 0.1 mole of chloroacetone in ethanol was run as indicated above. A crude yield of 11.0 g. of dihydrochloride of (V), m.p. 195–197°, resulted; two crystallizations from ethanol–hexane gave 7.4 g. (42%) of fine white needles, m.p. 215–216°. The base (V) was an oil.

Anal. Calcd. for $C_{12}H_{16}N_2S_3 \cdot 2HCl$: N, 7.84; S, 26.91; Cl^-, 19.84. Found:[2] N, 8.05; S, 26.97; Cl^-, 19.91.

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[1] R. Dahlbom, *Acta Chem. Scand.*, **5**, 690 (1951).

[2] Analyses by Mr. M. E. Auerbach and staff of the Analytical Laboratories of this Institute.

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Polarographic Behavior of 12-Ketosapogenins

BY CONSTANTINE RICCIUTI, C. O. WILLITS, M. E. WALL AND M. M. KRIDER

RECEIVED DECEMBER 19, 1951

Steroidal compounds containing α,β-unsaturated keto groups are polarographically reducible. Eisenbrand and Picher[1] and Sartori and Bianchi[2] found that steroids such as testosterone, progesterone, pregnenol-17-one-3 and desoxycorticosterone, are reducible at the dropping electrode in aqueous ethanol solutions and give waves which are proportional to concentration. The polarographic method was applicable only to the Δ^4-unsaturated-3-ketosteroids, for their saturated analogs did not give polarographic waves. Wolfe, Hershberg and Fieser[3,4] investigated Δ^1-cholestenone and found that it was reducible. All of these reducible compounds contain an α,β-unsaturated keto group. They also extended the polarographic method to include 17-ketosteroids and 20-ketosteroids by reaction of these steroids with Girard Reagent T to form polarographically reducible Girard derivatives.

There have been no previous reports on the polarographic behavior of 12-ketosapogenins which

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[1] J. Eisenbrand and H. Picher, *Z. physiol. Chem.*, **260**, 83 (1939).

[2] G. Sartori and E. Bianchi, *Gazz. chim. ital.*, **74**, 8 (1944).

[3] J. K. Wolfe, E. B. Hershberg and L. F. Fieser, *J. Biol. Chem.*, **136**, 653 (1940).

[4] J. K. Wolfe, E. B. Hershberg and L. F. Fieser, *ibid.*, **140**, 215 (1941).

TABLE I

IDENTIFICATION CHARACTERISTICS OF SAPOGENINS USED IN THIS STUDY

Sapogenin	Melting point, °C.[a] Genin	Melting point, °C.[a] Acetate	Specific rotation[b] Genin	Specific rotation[b] Acetate	Infrared absorption
Tigogenin	207–209	205–206	−70	−74	Carbonyl absent
Hecogenin	260–261	245–246	+ 7	− 5	Carbonyl max. at 1706 cm.$^{-1}$
Kammogenin	241–243	253–254	−54	−80	Carbonyl max. at 1714 cm.$^{-1}$
Manogenin	244–246	248–250	− 2	−42	Carbonyl max. at 1709 cm.$^{-1}$
9,11-Dehydromanogenin[c]	232–233	258–260	− 7.8	..	Carbonyl max. at 1676 cm.$^{-1}$ C=C max. at 1602 cm.$^{-1}$

[a] All melting point determinations made with the Kofler block. [b] Rotations determined at 25°, sodium lamp, concentrations between 8–10 mg./ml. [c] 95% pure, as estimated from ultraviolet and infrared absorption, with approximately 5% of a non-conjugated carbonyl sapogenin.

are important as precursors in steroid syntheses. The present method for the determination of polarographic behavior of these compounds allows the use of a non-aqueous medium consisting of a lithium chloride methanol–benzene electrolytic solution in which the 12-ketosapogenins are soluble.

Experimental

A Sargent Model XXI Polarograph was used to obtain the current–voltage curves. The capillary had t and m values of 1.35 seconds and 3.587 mg. per sec., respectively, which gave a capillary constant of 2.46 mg.$^{2/3}$sec.$^{-1/2}$. The m and t values were obtained in an open circuit, with the polarographic cell maintained at 25.0°, and with the capillary dipping into the non-aqueous electrolytic solution. The capillary constant at −1.80 volts under the above conditions was 2.38. This value has been used to calculate the diffusion current constant of the 9,11-dehydromanogenin.

The electrolytic cell was a modified Lingane H-cell[5] with a saturated calomel reference electrode. This cell had an open circuit resistance of 1175 ohms, and all half-wave potentials were corrected for *IR* drop. Half-wave potential readings were made against the saturated calomel electrode, and the polarograms were obtained at 25 ± 0.1°. The sapogenins were isolated and characterized by methods developed at this Laboratory.[6] Descriptive data for these compounds are presented in Table I. Thirty milliliters of the electrolytic solution, consisting of 0.3 *M* lithium chloride in a 50–50 (by volume) mixture of absolute methanol–benzene, was measured into the sample arm of the H-cell. The solution was degassed with high-purity nitrogen, and a polarogram was recorded. The sample was then added (10–40 mg.), and the solution was again degassed with nitrogen. A polarogram was recorded, and from the increase in wave height, the diffusion current of the reducible sapogenin was calculated.

TABLE II

POLAROGRAPHIC CHARACTERISTICS OF 9,11-DEHYDROMANOGENIN

Wt. sample per 40 ml.	Mole per liter	i_d, µa.	i_d/C	$i_d/Cm^{2/3}t^{1/6}$
0.0121	0.000885	4.76	5516	2.32
.0258	.001887	10.10	5489	2.31
.0390	.003019	15.70	5643	2.37

Results and Discussion

Tigogenin, which has no keto group, shows no polarographic reduction. Hecogenin and manogenin, both having a 12-keto group but no unsaturated linkage, show no reduction. Kammogenin, which has a 12-keto group and a Δ^5-unsaturated linkage, also does not reduce. However, 9,11-dehydromanogenin, which has both a 12-keto group and a conjugated unsaturated linkage, reduces at the dropping electrode with a half-wave potential of −1.72 volts *vs.* S.C.E. and has a diffusion current constant of 2.33. This diffusion current constant is similar to that found for other conjugated ketones in the non-aqueous electrolyte. Mesityl oxide, for example, has a diffusion current constant of 2.07. The reducibility of the 12-keto group of 9,11-dehydromanogenin in the non-aqueous electrolyte was expected because of the conjugated carbonyl group in this compound. Table II shows that the wave height of the 9,11-dehydromanogenin is directly proportional to concentration in the range studied (10 to 40 mg./30 ml.). The use of the lithium chloride non-aqueous electrolyte made possible the direct polarographic analysis of these water-insoluble steroidal compounds.

Acknowledgment.—The authors acknowledge the assistance of C. R. Eddy in obtaining the infrared data for the sapogenins.

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(5) C. O. Willits, C. Ricciuti, H. B. Knight and D. Swern, *Anal. Chem.*, in press.

(6) M. E. Wall, *et al.*, *J. Biol. Chem.*, in press.

(7) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

The Heat of Neutralization of Hydrogen–Bentonite

BY W. H. SLABAUGH

RECEIVED APRIL 5, 1952

Many clays undergo stoichiometric reactions with various types of reagents. Reactions which involve the base-exchange character of clays have been widely investigated and are adequately reviewed elsewhere.[1] In previous work[2] there was good indication that the exchangeable hydrogen which was present in electrodialyzed bentonite systems was of two principal types, namely, hydrogen ions in the adsorbed layer of the colloidal micelles and hydrogen ions at the base-exchange sites. Further, these ions showed primary and secondary characteristics comparable to a typical diprotic acid. The present work which consists of a thermodynamic study of the neutralization of these hydrogen ions gives good indication that there is a fundamental difference between these types of hydrogen ions and that, during storage, there is a definite tendency for the absorbed ions to become more intimately associated with the clay micelles.

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(1) E. A. Hauser, *Chem. Revs.*, **37**, 307 (1945); C. E. Marshall, "The Colloid Chemistry of the Silicate Minerals," Academic Press, Inc., New York, N. Y., 1949.

(2) W. H. Slabaugh and J. L. Culbertson, *J. Phys. Colloid Chem.*, **55**, 744 (1951).