It was found, however, that 8-quinolinol-5-sulfonic acid gave a catalytic wave in acid solutions at more negative potentials than did 8-quinolinol, so that at least one of the reduction waves prior to the catalytic wave could be analyzed (Fig. 1). Logarithmic analysis of this reduction wave indicated a one-electron process. Additional waves were masked by the catalytic wave.

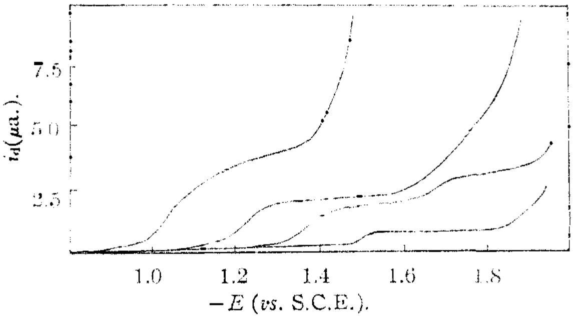

Fig. 1.—Polarograms of 8-quinolinol-5-sulfonic acid; from left to right: pH 3.75, 6.50, 8.90, 11.10; concentration 4.73×10^{-4} *M*.

In approximately neutral solutions 8-quinolinol-5-sulfonic acid was remarkably free from maxima, in contrast to 8-quinolinol.[1] The reduction wave found in acid solutions decreased in height with increasing pH. At a pH of 9 a well-defined double wave is obtained without indication of any following catalytic wave.

In alkaline solutions (pH 10–11.5) a single wave decreasing in height with increasing pH was obtained; the half-wave potential followed the equation $E_{1/2} = -0.77 - 0.059\ p\text{H}$. Evidently the reaction is a one-electron reduction similar to 8-quinolinol.

In stronger alkali (pH 12) 8-quinolinol-5-sulfonic acid was not reducible. The double negative charge on the ion in such solutions may prevent the acquisition of further electrons.

The behavior of 8-hydroxyquinaldine-5-sulfonic acid was also investigated; in most respects it resembled 8-quinolinol-5-sulfonic acid fairly closely. The half-wave potential in alkaline solutions obeyed the equation $E_{1/2} = -0.97 - 0.050\ p\text{H}$.

In view of the smoother waves obtained from these sulfonic acid derivatives in acid and neutral solutions they would seem to be better suited for analytical use than 8-quinolinol which has a usable reduction wave only in alkaline solution.

Experimental

A Sargent Model XXI Polarograph and an H-type cell kept at 25 ± 0.01° were employed for all determinations. Measurements were made against a saturated calomel electrode. The characteristics of the dropping mercury electrode, determined in 0.1 *N* potassium chloride on open circuit, were: m = 2.30 mg./sec., t = 4.00 sec.

Polarograms were run on each compound at six or more pH values between 2 and 12 and at concentrations ranging from 0.0001 to 0.001 *M*. Britton and Robinson buffers (consisting of acetic, phosphoric and boric acids with sodium hydroxide) were used after polarographic examination for reducible impurities. Oxygen was removed from the solutions with nitrogen. An instrument sensitivity of 0.100 was usually suitable.

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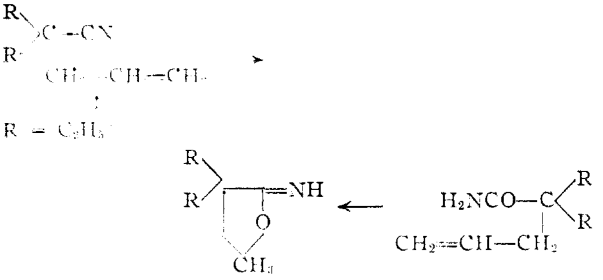
The Cyclization of Disubstituted Pentenoic Acid Derivatives

BY ROBERT F. RAFFAUF[1]

RECEIVED FEBRUARY 23, 1952

The conversion of substituted pentenoic acids to lactones, and of α-benzylpentenoic acid to a tetrahydronaphthalene derivative by means of sulfuric acid had been studied by Darzens some years ago.[2] More recent expression of interest in the cyclization of these acids[3] prompts us to record a similar series of observations with reference to the facile cyclization of 2,2-diethyl-4-pentenenitrile (I) which was carried out in these laboratories independently.

When I was dissolved in cold (0–5°) concentrated sulfuric acid and the solution was allowed to come to room temperature gradually (3–5 hr.) there was obtained, after dilution with water and neutralization with sodium hydroxide an 80% yield of a basic substance which, according to the observations of Schultz[4] and Easton,[5] we formulated as 2-imino-3,3-diethyl-5-methyltetrahydrofuran (II). The compound was surprisingly stable; it distilled with no evidence of decomposition as a colorless liquid (b.p. 80–82° (10 mm.)). *Anal.* Calcd. for $C_9H_{17}NO$: N, 9.02. Found: N, 8.80, 8.90.[6] It formed a crystalline benzenesulfonyl derivative, colorless needles from ethanol, m.p. 113–115°. *Anal.* Calcd. for $C_{15}H_{21}NO_3S$: N, 4.74; S, 10.85. Found: N, 4.68, 4.67; S, 10.80, 10.82. Hydrolysis in dilute mineral acid, or in alcoholic alkali followed by acidification, yielded a neutral, nitrogen-free product (b.p. 108–112° (19 mm.)) whose properties agreed with those expected for a lactone. *Anal.* Calcd. for $C_9H_{16}O_2$: C, 69.2; H, 10.3. Found: C, 68.8, 68.4; H, 10.2, 10.3. The same product was obtained from 2,2-diethyl-4-pentenoic amide (III); however, the solution of this compound in sulfuric acid was not strongly exothermic and could be conducted without external cooling. Craig's proposed mechanism[3] offers, in this case, a plausible description of the course of the reaction. In the case of the nitrile, however, this course is not as obvious; clearly an atom of oxygen must be introduced into the molecule to account for the product. Whether this is accomplished by initial and rapid hydrolytic attack of the CN-group followed by cyclization, or by preliminary addition of sulfuric acid to the allylic double bond followed by cyclic



II III

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[1] Research Associate, National Cancer Institute; present address: Smith, Kline and French Laboratories, Philadelphia 1, Pa.

(2) G. Darzens, *Compt. rend.*, **183**, 748, 1110 (1926).

(3) P. N. Craig, THIS JOURNAL, **74**, 129 (1952).

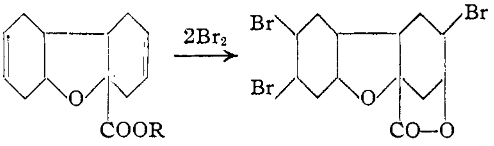
(4) E. M. Schultz, C. M. Robb and J. M. Sprague, *ibid.*, **69**, 2454 (1947).

(5) N. R. Easton, J. H. Gardner and J. R. Stevens, *ibid.*, **69**, 2941 (1947).

(6) Microanalyses by Mr. S. Alpert.

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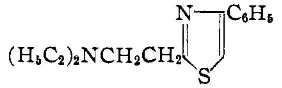
β,β'-Di-(2-thiazolyl)-diethyl Sulfides

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.



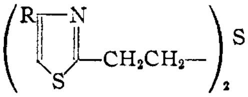
I

$(H_5C_2)_2NCH_2CH_2CSNH_2$

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).