Then

$$x_{21} = c_2 + \left(k_1c_1 - \frac{1}{3}k_2c_2 - 2k_3c_2^2\right)t$$

and

$$u_{11} = [1 - (a + bc_2)t]\left(k_1c_1 - \frac{1}{3}k_2c_2 - 2k_3c_2^2\right) - cc_2t,$$

etc.

This example was suggested by Mr. Manuel F. Morales of the Department of Physiology.

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The Influence of Electrolytes upon Ammonolysis by Liquid Ammonia

BY JOE F. LEMONS, P. M. WILLIAMSON, ROBBIN C. ANDERSON AND GEORGE W. WATT

Shatenshtein and Markova[1] have shown that the ammonolysis of pilocarpine by liquid ammonia is catalyzed markedly by certain salts and that the energy of activation for the catalyzed reactions is much greater than for reactions effected in the absence of catalysts. Similar results are obtained (Table I) when values for the energy of activation corresponding to the catalyzed ammonolysis of diethyl malonate and ethyl benzoate are calculated from data published by Audrieth and co-workers.[2,3] These data together with those

TABLE I

AMMONOLYSIS OF ESTERS

	Conc. of NH_4Cl, M	Energy of activation, cal./mole
Diethyl malonate	None	3500
	0.15	8300
Ethyl benzoate	.37	8000
	.75	8300

of Shatenshtein and Markova show that, for the ammonolysis of ester-type linkages by liquid ammonia, both the rate of reaction and energy of activation are increased by the presence of an electrolyte or by an increase in the concentration of such an electrolyte. In view of these results, it seemed desirable to secure values for the energy of activation under similar conditions for the ammonolysis of 2-chlorobenzothiazole (a reaction involving a halide-type bond), the rate of which has recently been shown to be but little influenced by the presence of electrolytes.[4]

Experimental

Reagent grade ammonium carbonate, ammonium sulfamate prepared as described by Baumgarten[5] and Audrieth,[6] and ammonium carbamate prepared as described by Basaroff[7] were used. Other materials and experimental methods were identical with those previously described.[4]

Results.—Data relating to the effect of certain salts upon the ammonolysis of 2-chlorobenzothiazole are summarized in Table II. Although in many cases the rate of reaction is increased slightly, the energy of activation is increased by all the electrolytes used. The results obtained using ammonium carbamate and ammonium carbonate constitute an exception to the recently published statement by Cheronis and Spitzmueller[8] to the effect that the "carbamate effect" is "of general application in ammonolytic reactions."

TABLE II

AMMONOLYSIS OF 2-CHLOROBENZOTHIAZOLE

Electrolyte	k_{298}, hours^{-1}	k_{303}, hours^{-1}	Energy of activation, cal./mole
NH_4Cl (0.314 M)	0.0185	0.0432	15,000
$NH_4O_2CC_6H_5$ (0.314 M)	.0175	.0431	15,900
$NH_4SO_3NH_2$ (0.314 M)	.0176	.0412	15,000
$NH_4CO_2NH_2$ (satd.)	.0163	.0395	15,700
$(NH_4)_2CO_3$ (satd.)	.0158	.0386	15,800
NaCl (0.314 M)	.0184	.0446	15,600
KCl (satd.)[a]	.0172	.0410	15,300
None	.0186	.0405	13,700

[a] We wish to call attention to the fact that in Table III of an earlier paper,[4] it should have been indicated that the potassium chloride solution used was *saturated*, and not 0.314 M.

Liquid ammonia is a solvent of comparatively low dielectric constant, and it would seem probable that salt effects in liquid ammonia solutions would be more pronounced than in aqueous solutions. Since in many cases concentration data, etc., are known only approximately, it is not possible to make quantitative calculations on interionic effects, etc., from data at present available. However, the differences in the energy of activation in the presence and in the absence of a catalyst are greater than the probable experimental errors. The rate measurements on the ammonolysis of diethyl malonate gave results which were reproducible only to within 10%, partly because of autocatalysis by the malonamide. The values

(1) Shatenshtein and Markova, *Acta Physicochim.* (U. S. S. R.), **11**, 131 (1939).

(2) Slobutsky, Audrieth and Campbell, *Proc. Nat. Acad. Sci.*, **23**, 611 (1937).

(3) Fellinger and Audrieth, THIS JOURNAL, **60**, 579 (1938).

(4) Lemons, Anderson and Watt, *ibid.*, **63**, 1953 (1941).

(5) Baumgarten, *Ber.*, **69**, 1929 (1939).

(6) Audrieth, *et al.*, *Chem. Rev.*, **26**, 49 (1940).

(7) Basaroff, *J. prakt. Chem.*, **I**, 283 (1870).

(8) Cheronis and Spitzmueller, *J. Org. Chem.*, **6**, 349 (1941).

in Table I were calculated using the data corresponding to those conditions under which this effect should be at a minimum, and even when the maximum possible error is assumed, the values for the energy of activation in the presence and in the absence of a catalyst are 7500 and 4300 cal./mole, respectively. For the ammonolysis of pilocarpine, ethyl benzoate, and 2-chlorobenzothiazole, data on the concentrations used, the reproducibility of results, etc., may be found in earlier publications.[1,3,4] Too much dependence may not be placed upon the results for ethyl benzoate because data on the energy of activation in the absence of a catalyst are not available.

Additional experimental studies on the rate and order of these reactions under conditions in which the concentration of the ester or halide and, especially, the concentration of catalyst are varied more widely will be necessary before definite conclusions may be drawn as to the nature of the effect involved. Nevertheless, although the absolute values of the energies of activation may be questionable in some cases, it is significant that for all ammonolytic reactions in liquid ammonia for which data are now available, the addition of electrolytes appears consistently to increase the energy of activation.

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Sterols. CXXXII. Sapogenins. LIV. The Action of Hydrogen Peroxide on the Pseudosapogenin Acetates and on the Pregnenolones

BY RUSSELL E. MARKER, ELDON M. JONES AND EMERSON L. WITTBECKER

Hydrogen peroxide in acetic acid reacts upon pseudosarsasapogenin[1] to give a neutral compound of the formula $C_{27}H_{44}O_5$. Under similar conditions sarsasapogenin acetate[1] gives pregnanetriol-3(β),16,20, resulting from rupture of the side-chain between C_{20} and C_{22}. We have treated pseudosarsasapogenin diacetate in acetic acid with hydrogen peroxide and have obtained Δ^{16}-pregnenol-3(β)-one-20 acetate, which was produced by splitting of the side-chain between C_{20} and C_{22}. Likewise, pseudotigogenin diacetate gave Δ^{16}-*allo*-pregnenol-3(β)-one-20 acetate. The reaction of hydrogen peroxide in acetic acid upon Δ^{16}-pregnenol-3(β)-one-20 acetate and Δ^{16}-*allo*-pregnenol-3(β)-one-20 acetate gave a good yield of an unidentified crystalline product. These experiments show that the pregnene compounds are not formed as a direct oxidation product of the pseudosapogenins, but that an intermediate is first formed which requires hydrolysis to give the pregnene derivative.

We wish to thank Parke, Davis and Company for their generous help.

Experimental Part

Treatment of Pseudosarsasapogenin Diacetate with Hydrogen Peroxide.—Pseudosarsasapogenin, 3 g., was converted to the acetate by refluxing with acetic anhydride. The residue from the evaporation of the excess anhydride was dissolved in 200 cc. of acetic acid, and 30 cc. of 30% hydrogen peroxide was added. The mixture was heated to 70° for five hours, then concentrated by evaporation *in vacuo* and poured into water. The mixture was extracted with ether and the extract was washed with water. The ether was evaporated and the residue was hydrolyzed with boiling methanolic potassium hydroxide. The neutral fraction melted at 180–183° after crystallization from aqueous methanol.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 7.97; H, 10.2. Found: C, 79.7; H, 10.2.

With boiling acetic anhydride this substance gave an acetate which melted at 140–141° after crystallization from aqueous methanol. It gave no depression in melting point when mixed with an authentic sample of the acetate of Δ^{16}-pregnenol-3(β)-one-20.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.0; H, 9.6. Found: C, 77.0; H, 9.4.

Treatment of Pseudotigogenin Diacetate with Hydrogen Peroxide.—A mixture of 10 g. of pseudotigogenin diacetate, 50 cc. of 30% hydrogen peroxide, and 500 cc. of acetic acid was heated to 70° for six hours. Water was added and the mixture was extracted with ether. The extract was washed with water and the ether was evaporated. The residue was hydrolyzed with hot methanolic potassium hydroxide, poured into water, and extracted with ether. The extract was washed with water and the ether was evaporated. The residue was refluxed with excess acetic anhydride and the excess solvent was evaporated *in vacuo*. The residue was crystallized from methanol and the first fraction, which appeared to be a mixture, was discarded. The second fraction melted at 159–162° and did not depress the melting point of an authentic sample of the acetate of Δ^{16}-*allo*-pregnenol-3(β)-one-20.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.0; H, 9.6. Found: C, 77.1; H, 9.7.

Treatment of Δ^{16}-Pregnenol-3(β)-one-20 Acetate with Hydrogen Peroxide.—A mixture of 5 g. of Δ^{16}-pregnenol-3(β)-one-20 acetate, 250 cc. of acetic acid, and 50 cc. of 30% hydrogen peroxide was heated to 70° for five hours. The solvent was partially evaporated *in vacuo* and the remainder was dissolved in ether. The solution was washed with water and dilute sodium carbonate solution. Acidification of the alkaline wash gave no acids. The ether solution was washed with water and the ether was evapo-

(1) Marker, Jones and Krueger, THIS JOURNAL, **62**, 2532 (1940).