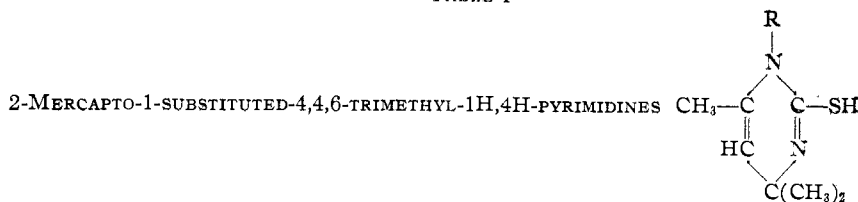


TABLE I



Compd. ^a	R	Derived from	M. p., °C. ^b	Yield, % ^c	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
1	Amino	Hydrazine	209-210	80	C ₇ H ₁₃ N ₃ S	49.09	49.11	7.65	7.70	24.54	24.57
2	<i>p</i> -Aminophenyl	Phenylhydrazine	170-171	95	C ₁₃ H ₁₇ N ₃ S	63.12	63.33	6.93	6.93	16.99	16.73
3	Methyl ^d	Methylamine	86-87	..	C ₈ H ₁₄ N ₂ S	56.43	56.47	8.29	8.17	16.46	16.42
4	Ethyl	Ethylamine	148-149	78	C ₉ H ₁₆ N ₂ S	58.65	58.75	8.75	8.87	15.20	15.13
5	<i>n</i> -Butyl	<i>n</i> -Butylamine	113-114	70	C ₁₁ H ₂₀ N ₂ S	62.21	62.28	9.50	9.57	13.19	13.11
6	Allyl ^e	Allylamine	129-130 ^f	..	C ₁₀ H ₁₆ N ₂ S	61.18	61.10	8.22	8.28	14.27	14.11
7	3-Isopropoxy- propyl	3-Isopropoxy- propylamine	84-85	50	C ₁₃ H ₂₄ N ₂ OS	60.89	60.77	9.43	9.54	10.93	10.87
8	<i>p</i> -Nitrophenyl	<i>p</i> -Nitroaniline	201	75	C ₁₃ H ₁₄ N ₃ O ₂ S	56.30	56.41	5.45	5.53	15.15	14.70
9	2,4-Dichlorophenyl	2,4-Dichloroaniline	203-204	78	C ₁₃ H ₁₄ Cl ₂ N ₂ S	51.83	51.88	4.68	4.72	9.30	8.99
10	<i>o</i> -Mercaptophenyl	<i>o</i> -Aminobenzene- thiol	172-173	79	C ₁₃ H ₁₆ N ₂ S ₂	59.05	59.19	6.10	6.16	10.60	10.60
11	<i>p</i> -Hydroxyphenyl	<i>p</i> -Aminophenol	200	86	C ₁₃ H ₁₆ N ₂ OS	62.88	62.74	6.50	6.56	11.29	11.19
12	<i>p</i> -Anisyl	<i>p</i> -Anisidine	189	41	C ₁₄ H ₁₈ N ₂ OS	64.09	64.15	6.91	6.98	10.68	10.62
13	<i>p</i> -Acetylphenyl	<i>p</i> -Aminoaceto- phenone	189	78	C ₁₅ H ₁₈ N ₂ OS	65.66	65.65	6.61	6.46	10.21	10.11
14	Benzyl	Benzylamine	181-182	87	C ₁₄ H ₁₈ N ₂ S	68.25	68.35	7.36	7.40	11.37	11.20
15	Furfuryl	Furfurylamine	126-127	86	C ₁₂ H ₁₆ N ₂ OS	60.98	61.03	6.83	6.73	11.86	11.79
16	<i>p</i> -(α -Phenyliso- propyl)-phenyl	<i>p</i> -(α -Phenyliso- propyl)-aniline	173-175	76	C ₂₂ H ₂₆ N ₂ S	75.38	75.55	7.48	7.36	7.99	7.93

^a Compounds 2 and 13 were recrystallized from benzene; 3,7 from hexane; all others from ethanol. ^b Melting points are for analytical samples and are uncorrected. ^c Yields are based on crude products. ^d The intermediate, 1-(1,1-dimethyl-3-oxobutyl)-3-methyl-2-thiourea, obtained in 93% yield, and melting at 161° (with decomposition) after recrystallization from hexane, was the initial product. *Anal.* Calcd. for C₉H₁₆N₂OS: C, 51.03; H, 8.57; N, 14.88. Found: C, 50.64; H, 8.48; N, 14.64. ^e The intermediate, 1-(1,1-dimethyl-3-oxobutyl)-3-allyl-2-thiourea, obtained in 83% yield, and melting at 138° after recrystallization from alcohol, was the initial product. *Anal.* Calcd. for C₁₀H₁₈N₂OS: C, 56.04; H, 8.46; N, 13.07. Found: C, 56.01; H, 8.39; N, 13.06. W. Traube and H. Lorenz, *Ber.*, **32**, 3156 (1899), reported a melting point of 138°. ^f W. Traube and H. Lorenz, *ibid.*, **32**, 3156 (1899), reported a melting point of 130°.

Experimental

2-Mercapto-1-substituted-4,4,6-trimethyl-1H,4H-pyrimidine. **Typical Preparation.**—Ethylamine (45 g., 1 mole) was added as a 25% aqueous solution,⁵ over a period of 15 minutes, to a vigorously agitated mixture of 157 g. (1 mole) of 2-methyl-2-isothiocyano-4-pentanone, 300 ml. of water and 5 ml. of hydrochloric acid. The reaction mixture was heated to reflux and after cooling to room temperature, the product which precipitated was filtered, washed with water and dried.

In two instances (Table I, compounds 3 and 6) the products initially obtained were the intermediate thioureas. By heating these intermediates with an excess of 25% sulfuric acid, ring closure was effected to give the corresponding pyrimidines.

Acknowledgment.—The analyses of all compounds were made by J. R. Kubik and A. K. Kuder.

(5) Water dilution is advantageous in controlling the reaction rate when employing water soluble amines and hydrazines.

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Crystalline Sodium Lactobionate Monohydrate

BY GEORGE E. N. NELSON AND FRANK H. STODOLA
RECEIVED DECEMBER 4, 1952

The study and utilization of the bionic acids have been hampered by the lack of salts which can be readily purified by crystallization. After many attempts Isbell¹ was able to prepare crystalline cal-

cium lactobionate, but unfortunately its gelling tendency made it of little use in purification. Recently we succeeded in preparing crystalline sodium lactobionate and find it to be readily obtainable in the pure state as a monohydrate which filters easily and is stable to heat.

Experimental

Calcium lactobionate, prepared by the oxidation of lactose by *Pseudomonas graveolens*,² was converted to the sodium salt by reaction with the calculated amount of sodium oxalate. The filtered solution was brought to incipient cloudiness by the addition of alcohol and then stirred with seed crystals. More alcohol was then added and the crystals, which filtered rapidly, were washed successively with 70% alcohol, absolute alcohol and ether. For analysis, this product was recrystallized as follows: One gram was dissolved in the minimum amount of water (2.5 ml.) at room temperature. After addition of more water (0.5 ml.) 3 ml. of 95% alcohol was added gradually. Seed crystals were added and the solution stirred vigorously for several minutes. On standing at room temperature, clusters of bars crystallized out. After 1 day at room temperature and another day in the refrigerator, the crystals (810 mg.) were filtered off and washed as described above. After drying in a vacuum desiccator (20 mm., 25°) for a day, the compound lost no further weight at 78° (1 mm.); it was then analyzed.

Anal. Calcd. for C₁₂H₂₁O₁₂Na·H₂O: C, 36.18; H, 5.82; Na, 5.77; H₂O, 4.51. Found: C, 36.1; H, 5.81; Na, 5.92; H₂O (Karl Fischer Method), 4.7.

A sample dried to constant weight at 140° (1 mm.) lost only 0.3% of its weight.

(2) F. H. Stodola and L. B. Lockwood, *J. Biol. Chem.*, **171**, 213 (1947).

(1) H. S. Isbell, *Bur. Stand. J. Res.*, **11**, 713 (1933).

Heated in a capillary tube, the monohydrate evolves gas rapidly at 175° (cor.) and increases in bulk about twentyfold. It shows a rotation of $[\alpha]^{24D} +22.3^\circ$ (c 5, H₂O).

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(3) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

Acid-catalyzed Hydrolysis of Ethyl Acetate

BY OGDEN R. PIERCE AND GEORGE GORIN

RECEIVED NOVEMBER 10, 1952

In connection with other work done in this Laboratory, it was of interest to measure the rates of hydrolysis of ethyl acetate at 25° in aqueous acetone (70% by volume) with varying concentrations of hydrochloric acid as catalyst, and also to estimate the relative catalytic activities of trifluoroacetic and difluoroacetic acids. The results are reported in Table I, together with data from the literature from which interesting comparisons can be made. Each value determined in this investigation is the average of three or four determinations, and the degree of reproducibility is indicated by the indeterminate error of the mean.¹ The ester concentration was 0.2 *M* unless otherwise specified in the footnote.

TABLE I

Concn. catalyst, <i>c</i> , mole/l.	Medium	Cat. constant, <i>k/c</i> , × 10 ⁵ , l. mole ⁻¹ sec. ⁻¹
0.025 <i>N</i> HCl	70% acetone	4.24 ± 0.05
.05 <i>N</i> HCl ²	70% acetone	4.27 ± .01
.1 <i>N</i> HCl	70% acetone	4.28 ± .04
.5 <i>N</i> HCl ³	70% acetone	4.61
.1 <i>N</i> CF ₃ COOH	70% acetone	1.90 ± 0.02
.1 <i>N</i> HCl ⁴	Water	10.8
.1 <i>N</i> CF ₃ COOH	Water	10.0 ± 0.1
.1 <i>N</i> CHF ₂ COOH	Water	6.09 ± 0.05
.1 <i>N</i> CCl ₃ COOH ⁵	Water	10.7
.1 <i>N</i> CHCl ₂ COOH ⁶	Water	6.30

It is seen that the reaction-rate constant divided by the concentration of catalyzing acid is constant within experimental error for 0.1, 0.05 and 0.025 *N* hydrochloric acid. This indicates that the rate is proportional to the concentration of catalyst within this concentration range. The catalytic constant is somewhat lower than the value previously found by Haskell and Hammett³ in 0.5 *N* acid, and this is wholly analogous to the results reported for water, where the catalytic constant

(1) F. Daniels, *et al.*, "Experimental Physical Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1949, p. 357.

(2) G. Davies and D. P. Evans, *J. Chem. Soc.*, 339 (1940), reported 4.47×10^{-5} at 24.8° and correction to 25.0° using their value for the energy of activation gives 4.55×10^{-5} . In their experiments the ester concentration was 0.05 *M* and the medium contained about 1.5 ml. more water per 100 ml. of solution: the higher water content is sufficient to account for the difference in rates. The rate found by the present authors for 0.1 *M* ester in a medium containing about 1 ml. more water was 4.60×10^{-5} .

(3) V. C. Haskell and L. P. Hammett, *THIS JOURNAL*, **71**, 1284 (1949).

(4) H. M. Dawson and W. Lowson, *J. Chem. Soc.*, 2146 (1928).

(5) H. S. Taylor, *Medd. K. Vetenskapsakad. Nobelinst.*, **2**, No. 37, 1-18 (1913).

(6) H. M. Dawson and W. Lowson, *J. Chem. Soc.*, 1217 (1929).

is 1.08×10^{-4} throughout the range 0.0002 to 0.1 *N* hydrochloric acid, and shows a 5% increase in 0.5 *N* acid.⁴

In 70% acetone at 0.1 *N* concentration, trifluoroacetic acid is less than half as effective as hydrochloric acid, and this must reflect the relative strength of these acids, although the relation is not linear. In water, a medium of much higher dielectric constant, the levelling effect of the solvent⁷ makes the difference less marked; hydrochloric acid, trifluoroacetic acid and trichloroacetic acid all appear to be about equally strong. Even in water, however, difluoroacetic acid is weaker than any of these, and about as good a catalyst as dichloroacetic acid.

Experimental

Materials.—Ethyl acetate was a commercial C.P. product, which was purified according to Weissberger and Proskauer⁸ and distilled through a 4-ft. helices-packed Todd column; the middle third boiled within 0.1° and was collected in three successive fractions which were employed interchangeably with no noticeable change in results. A portion of this product was purified again in the same way and a small center cut was collected at constant temperature. The results obtained with this preparation were the same as the rest within experimental error.

Trifluoroacetic acid was obtained from the Minnesota Mining and Mfg. Co. and distilled twice; a small center fraction was collected for use each time, and both preparations gave the same results: b.p. 70-71°, neut. equiv. 113.7 (calculated 114.0). Difluoroacetic acid was a laboratory preparation, redistilled from phosphorus pentoxide: b.p. 133.2°, neut. equiv. 95.6 (calculated 96.0).

Acetone was a C.P. product that was refluxed with potassium permanganate and distilled, the center four-fifths being retained for use. The "70% acetone" medium consisted of 70.0 ml. of acetone (54.9 ± 0.1 g.) per 100 ml. of solution.

Method.—Water and other reagents were first allowed to come to constant temperature. Two milliliters of ester was then placed in a weighed 100-ml. volumetric flask containing a little water, and the weight of the ester was determined by difference; the initial concentration of ester, *a*, was calculated from this weight. Water, acetone if desired, and appropriate amounts of acid were then added to the flask and the solution diluted to the mark. Immediately after mixing and at appropriate intervals thereafter 2.00-ml. aliquots were withdrawn, diluted to 20 ml. with water, and titrated with standard 0.01 *N* barium hydroxide to a phenolphthalein end-point. Zero time was taken as the instant at which the acid was added, and the titer at zero time was estimated by extrapolation. The concentration of catalyzing acid could thus be estimated directly, and the value compared to that calculated from the normality of the original solution and the dilution factor; an average of the two values was taken as the actual catalyst concentration. The amount of ester, *x*, hydrolyzed at any time, *t*, was calculated from the titer of barium hydroxide required in excess of the extrapolated zero-time titer. Measurements were made only in the interval to 50% reaction, so that the effect of the reverse reaction could be neglected. The reaction rate constant was then computed by means of the equation⁹

$$k = \frac{2.303}{t_2 - t_1} \log \frac{(a - x_1)}{(a - x_2)}$$

taking care to vary the intervals of time between successive measurements. Usually five or six values of *k* were obtained in each experiment, and the results averaged.

(7) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 256.

(8) A. Weissberger and E. Proskauer, "Organic Solvents," Oxford University Press, 1935, p. 150.

(9) W. E. Roseveare, *THIS JOURNAL*, **53**, 1651 (1931). As pointed out in this article, the more popular alternative form of the equation, *i.e.*, $k = 2.303/t \log (a/a - x)$, gives greater statistical weight to the first measurements, which would be particularly undesirable in this case because the first titers are small differences between large numbers.