duced by the action of chlorine on 1,1-dichlorocyclopropane.[2]

In the course of a fundamental study of the properties of the chloropropanes, we have prepared and characterized the missing 1,1,3,3-tetrachloropropane. The final step was the chlorination of 1,1,3-trichloropropane followed by fractionation to separate the three possible tetrachlorides, 1,1,1,3-, b.p. 157.5°; 1,1,3,3-, b.p. 162°; 1,1,2,3-, b.p. 178.3°.

Experimental

1,1,3-Trichloropropane was prepared, independently of, but by a method similar to that of Stitz,[3] from β-chloropropionaldehyde and PCl_5. Eight moles (1180 g.) of this trichloride diluted with 1000 g. of carbon tetrachloride was chlorinated at 55–60° in a two-liter flask fitted with a gas dispersion disc, stirrer, thermometer and condenser. Chlorine was passed in slowly until the gain in weight was 221 g., corresponding to 80% monochlorination, 10 hours being required for this operation. The reaction mixture was distilled using a 2.5 × 100 cm. column packed with glass helices, at atmospheric pressure until the carbon tetrachloride was removed and finally at 100 mm. pressure. The yield of 1,1,3,3-tetrachloropropane, boiling range 94–98° (100 mm.) was 320 g. or 30%. Properties of the purified material were: b.p. 161.9° (756 mm.); f.p. −27° (uncor.); d^{20}_4 1.4689; d^{25}_4 1.4612; n^{20}_D 1.4848; n^{25}_D 1.4813.

Anal. Calcd. for $C_3H_4Cl_4$: Cl, 77.97. Found: Cl, 77.19.

Acknowledgment.—The authors are grateful to Miss Darien Dorn and Mr. R. J. Breazeale who assisted in this work.

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[2] P. G. Stevens, THIS JOURNAL, **68**, 620 (1946).

[3] F. Stitz, *Österr. Chem.-Ztg.*, **48**, 186 (1947); *C. A.*, **44**, 7226 (1950).

DEPARTMENT OF CHEMISTRY
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RECEIVED OCTOBER 5, 1950

Reciprocal Solubility of 4,6-Dimethyl-1,2-pyrone and Water

BY RICHARD H. WILEY AND NEWTON R. SMITH

In studies involving reaction of 4,6-dimethyl-1,2-pyrone in water solution, it was observed that this unsaturated lactone possessed lower and upper consolute temperatures between 0 and 100°. Although this compound has been known for a number of years,[1] no comment has been made on this phenomenon. This report presents data on the solubility of 4,6-dimethyl-1,2-pyrone in water which establish upper and lower consolute temperatures.

The occurrence of an upper and lower consolute temperature of organic compounds in water solution has been observed in only a few cases; these compounds include amines,[2] ketones,[3] alcohols[4] and glycol monoethers.[5] This apparently is the first reported occurrence of both upper and lower consolute temperatures for an ester or lactone. The solubility relations between 4,6-dimethyl-1,2-pyrone and water are unusual for this reason and also because the region which consists of two phases occupies such a small area on the phase diagram. The lower and upper consolute temperatures are 59.7 ± 0.5° and 86.3 ± 0.5°, respectively, as shown in Fig. 1. In systems containing concentrations below 25% and above 50% of the pyrone by weight, the two liquids are completely miscible above 51.5°, the melting point of the pyrone. At room temperature the solid pyrone crystallizes from sufficiently concentrated solutions slowly on standing or rapidly if seeded with the pyrone.

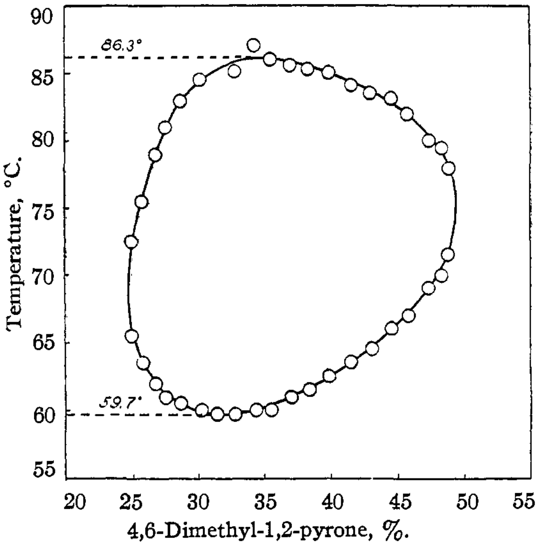

Fig. 1.—The 4,6-dimethyl-1,2-pyrone–water system.

Within the accuracy of the experiment the solubility curve is smooth except for one point on the higher solution curve when an upper consolute temperature of 87° was obtained at a concentration of 34.3% pyrone. The temperatures were read at a point of definite separation of phases. This separation was preceded by a marked opalescence. The exact temperature at which the opalescence occurs was difficult to determine and was obscured by a change from a water white to a yellow color as the experiment progressed.

The usual explanation for this phenomenon is that below the lower critical temperatures compound formation of the hydrogen bond type increases the solubility of the organic compound.[6] This is probably the explanation of the solubility behavior of the dimethylpyrone. There is a possibility that since the dimethylpyrone is easily hydrolyzed the phenomenon may be due to a reversible hydrolysis of the lactone to the corresponding acid. This requires that the pyrone precipitate from cold and the acid from hot solutions. This is not too likely as one would expect the acid to be soluble in the concentration ranges involved at the high temperatures and it is known that the solubilities of ethyl ether and ethyl acetate increase with decreasing temperature.

Experimental

4,6-Dimethyl-1,2-pyrone, prepared by the decarboxylation of isodehydroacetic acid,[1] was distilled repeatedly and

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[1] Hantzsch, *Ann.*, **222**, 9 (1883).

[2] Flaschner, *J. Chem. Soc.*, **95**, 668 (1909).

[3] Kohnstamm and Timmermans, *Verslag Akad. Wetenschappen Amsterdam*, **21**, 783 (1913).

[4] Timmermans, *Arch. Néerland sci.*, **6**, 147 (1922).

[5] Cox, Nelson and Cretcher, THIS JOURNAL, **49**, 1080 (1927).

[6] Glasstone, "Textbook of Physical Chemistry," second ed., D. Van Nostrand Company, Inc., New York, N. Y., 1946, p. 728.

stored in a vacuum desiccator over calcium chloride. The pyrone melted at 51° (reported 51.5°).

A weighed amount of the pyrone was placed in a 50-ml. flask equipped with a stirrer and a cork stopper. The flask was placed in a water-bath with a thermometer and stirrer. Weighed quantities of freshly distilled water were added from a weighing bottle, the water-bath heated above the upper consolute temperature, and the bath allowed to cool slowly, during which time the upper and lower solution temperatures were recorded; then more water was added and the procedure repeated. These temperatures were reproducible within ±0.5°. Readings were recorded at the temperature at which there was a definite separation into two phases. The data are plotted in Fig. 1.

Acknowledgment.—The authors wish to thank the Research Corporation for a grant made in support of a program under which this work was done.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF LOUISVILLE
LOUISVILLE, KENTUCKY
RECEIVED NOVEMBER 6, 1950

COMMUNICATIONS TO THE EDITOR

NEOMYCINS B AND C, AND SOME OF THEIR DEGRADATION PRODUCTS

Sir:

In the course of purification of the antibiotic complex termed neomycin by Waksman and Lechevalier,[1] we have obtained by chromatography of the hydrochloric acid salt[2] in 80% methanol over alumina two homogeneous biologically active fractions. One of these closely resembles the neomycin B described by Regna and Murphy,[3] while the properties of the other, named by us neomycin C, sharply differentiate it from neomycin A[4] (see Table I).

TABLE I

COMPARISON OF PROPERTIES OF NEOMYCINS

	Neomycin component B, amorphous hydrochloride	Neomycin component C, amorphous hydrochloride	Neomycin A[4] amorphous hydrochloride	Neomycin B[3] amorphous sulfate
Biopotency in[a] nutrient broth *vs. Klebsiella pn.*	265 units/mg.	180 units/mg.	20 units/mg.[b]	260 255 units/mg.
Biopotency on nutrient Agar *vs. B. subtilis*	86 units/mg.	121 units/mg.	1700 units/mg.[b] 710 units/mg.[b]	....
$[\alpha]_D$	+54°	+80°	+83°	+58°

[a] The units are based on a comparison with a Waksman standard preparation. [b] These values determined with a sample of neomycin A hydrochloride kindly supplied by Dr. Karl Folkers.

Crystalline reineckates, picrolonates and *p*-(*p'*-hydroxyphenylazo)-benzenesulfonates have been prepared from both entities. In addition, antibacterially inactive, crystalline N-acetates have been obtained (*Neomycin B N-acetate*, needles from aqueous acetone; m.p. 200–205° with decomposition, after darkening and softening 186–190°; $[\alpha]^{22}D$ +62°, 0.4% in water. *Anal.* Found:[5] C, 50.71; H, 6.95; N, 9.45; acetyl, 32.4. *Neomycin C N-acetate*, needles from aqueous acetone; m.p. similar to that of neomycin B N-acetate, but showing a depression of 10° in mixed melting point determination; $[\alpha]^{22}D$ +90°, 0.4% in water. *Anal.* Found: C, 51.09; H, 7.47; N, 9.24; acetyl, 32.7). These data suggest that the two bases may be isomeric. All the nitrogen atoms are present as primary amino groups (Van Slyke).

Methanolysis of the hydrochlorides afforded the following two fragments:

(1) An amorphous hydrochloride, identical from both neomycin B and C, which was devoid of reducing power and yielded all its nitrogen as amino nitrogen in the Van Slyke determination. The empirical formula, $C_9H_{19}O_5N_3\cdot 3HCl$, may be derived from the analyses of the following crystalline derivatives. *N-acetate*, needles from methanol; decomposes *ca.* 300° without melting, after sintering at 260°; $[\alpha]^{22}D$ +88°, 0.3% in water. *Anal.* Calcd. for $C_9H_{16}O_5N_3(COCH_3)_3$: C, 48.00; H, 6.71; N, 11.20; acetyl, 34.4. Found: C, 47.76, 47.94; H, 6.95, 7.76; N, 11.46; acetyl, 36.5. *N-Benzoate*, needles from aqueous methanol, decomposes to black tar at 299–300° after darkening at 270°; $[\alpha]^{22}D$ +70°,0.5 % in methanol. *Anal.* Calcd. for $C_9H_{16}O_5N_3(COC_6H_5)_3$. C, 64.16; H, 5.57; N, 7.48. Found: C, 64.54; H, 6.02; N, 7.43. *Heptaacetate*, prisms from acetone, dried sample softens at 165°, undergoes transition 190–215°, liquifies at 260–262°; the cooled and solidified material (needles) then melts (without transition) at 262–265°; $[\alpha]^{22}D$ +49°, 0.5% in methanol. *Anal.* Calcd. for $C_9H_{12}O_5N_3(COCH_3)_7$ (mol. wt., 5.44): C, 50.83; H, 6.12; N, 7.73; total acetyl,

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[1] S. A. Waksman and H. A. Lechevalier, *Science*, **109**, 305 (1949).

[2] The crude neomycin preparations used were produced by the Divisions of Microbiological and Chemical Development, E. R. Squibb & Sons, New Brunswick, N. J.

[3] P. P. Regna and F. X. Murphy, THIS JOURNAL, **72**, 1045 (1950).

[4] R. Peck, C. E. Hoffhine, P. Gale and K. Folkers, *ibid.*, **71**, 2590 (1949).

[5] All analytical determinations were carried out by Mr. J. F. Alicino, Microanalytical Laboratory, E. R. Squibb & Sons, New Brunswick, N. J.