

The Melting Point of Nicotinic Acid*

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Within comparatively recent years, various investigators have reported widely different melting points for nicotinic acid, ranging from a value of 230–232° C. by McElvain, Conant and Corson (1) to 236–237° C. by Späth and Spitzer (2), while still more recent workers have obtained values as high as 238–239° C. (personal communication to the authors). The U. S. Pharmacopœia XI (3) states that "nicotinic acid melts between 234° and 237° C.," which is a rather wide range for a substance specified to have a purity of "not less than 99.5%."

In order to clarify these discrepancies an investigation was undertaken of the melting points of samples of nicotinic acid U. S. P. supplied by different manufacturers. In addition, one of the samples was subjected to six different purification steps, as outlined below, the melting point being checked after each step.

EXPERIMENTAL

Apparatus and Method.—Because of the difficulty encountered in regulating the U. S. P. melting-point apparatus to the desired temperature rise of $\frac{1}{2}$ ° C. per minute, a much larger mechanically stirred liquid bath was used and it was heated electrically rather than by a free flame. The bath consisted of a 1500-cc. beaker filled with coconut oil, this oil darkening less on repeated heating than other oils such as cottonseed, peanut or corn. Five turns of $\frac{1}{16}$ -inch wide nichrome ribbon were wound around the lower third of the beaker and kept in place with a cement made from asbestos fiber and water glass. The current through the ribbon was controlled by a rheostat. The oil was vigorously stirred by a motor-driven laboratory stirrer. With this set-up, the temperature rise of $\frac{1}{2}$ ° C. per minute in the neighborhood of the melting point could be maintained with ease.

The thermometer used was an Anschutz type having a range from 200° to 270° C., graduated in 0.2°, and certified by the United States Bureau of Standards to have a correction of +0.1 at 225.0° C. and 0.0 at 250.0° C. for total immersion of bulb and

liquid column. After checking against an auxiliary thermometer at 225°, 230°, 235° and 239° C., and obtaining consistent readings throughout this range on both thermometers, it was assumed that the Bureau of Standards thermometer gave correct readings in the range 230–240° C. The melting points were always determined with bulb and liquid column completely immersed in the oil, thereby eliminating the necessity for making an exposed stem correction.

The capillary tubes were carefully selected to have an internal diameter of 1.0 ± 0.1 mm., and a wall thickness of about 0.1 to 0.2 mm. They were filled to a height of 3 mm. after firmly tapping down. (The samples of nicotinic acid were all in the form of fine powders.) The capillaries were fastened to the thermometer with fine copper wire and were always long enough to stick out above the surface of the oil for a distance of several centimeters, even though the thermometer itself was totally immersed as regards bulb and liquid column.

In determining the melting point the temperature was raised rapidly to about 210° C., then heating was continued at approximately 3° C. per minute until the temperature was about 232° C., and from that point on heating was continued at exactly $\frac{1}{2}$ ° per minute until the melting was complete. The rate of heating was always checked with a stopwatch because a faster rise tends to give high values. The total time required for the determination was usually about one-half hour. Three readings were taken of the melting. First, the point at which the substance just began to soften, shrink or collapse, with no meniscus as yet visible; second, the point at which a clear meniscus could be seen and both solid and liquid were present in approximately equal amounts; third, the point at which all the solid had just melted and the liquid was completely clear. These points will be referred to as beginning, middle and end of melting, respectively.

Nicotinic Acids.—Samples of U. S. P. quality supplied by four different manufacturers were used. These will be referred to as Nicotinic Acid A, B, C and D.

Sample D, considered to be an excellent commercial sample, was subjected to the following successive steps of purification:

I. Recrystallization from water (1 in 15) after treatment with 1% Norite. Dried at 80° C.

II. Recrystallization of I from absolute alcohol (1 in 30) after treatment with 2% Norite. Dried at 80° C.

III. Dissolved II in water containing slightly more than an equivalent weight of sodium hydroxide, treated the solution with 1% Norite and evaporated until crystallization occurred. The sodium nicotinate was filtered off, washed with water and alcohol. It was then redissolved in water and hydrochloric acid added until the pH was 3.5. The precipitated nicotinic acid was filtered, washed and dried at 100° C.

IV. Nicotinic acid III was dissolved in hot concentrated hydrochloric acid and the solution allowed

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to cool and crystallize. The nicotinic acid hydrochloride was washed with water and air dried. It was then dissolved in water and sodium hydroxide added until the pH was 3.5. The precipitated nicotinic acid was washed and dried at 85° C.

V. Nicotinic acid IV was recrystallized from absolute alcohol (1 in 25). Dried at 80° C.

VI. Nicotinic acid V was sublimed *in vacuo*, heating in an oil bath at about 235° C.

These purified samples will be referred to as Nicotinic Acid I, II, III, IV, V and VI, respectively.

All of the samples were used as fine powders and all were dried in a desiccator over sulfuric acid for at least 24 hours before taking the melt. It was found, however, that this drying had no effect on the melting point, nor did drying at 100° C. for two hours have any effect.

Table.—Melting Point Data

Nicotinic Acid	Melting Point, ° C.		
	Beginning	Middle	End
A	232.0	235.9	236.5
B	232.0	235.9	236.5
C	231.8	235.5	236.4
D	232.2	236.0	236.6
I	232.0	236.0	236.4
II	232.0	236.0	236.6
III	232.0	235.8	236.2
IV	232.0	235.8	236.4
V	232.0	236.1	236.6
VI	231.0	236.1	236.6

It will be seen that all the commercial and purified samples melt over the same ranges, and that further purification of *D* by various methods which should have removed impurities did not change the melting point, indicating that the commercial material is already highly pure.

Although all of the samples softened at about 232° C., this temperature should not be considered as being in the melting range since no liquid melt will form at this temperature within a reasonable time. The true melting point where solid and liquid are in equilibrium probably lies between 235.5° and 236.6° C.

The low value obtained by McElvain, Conant and Corson (1) is probably due to the presence of nitro compounds obtained in the action of nitric acid on nicotine (4). The value of 236–237° C. reported by Späth and Spitzer (2) who sublimed their material *in vacuo* is substantially in agreement with our values.

In view of the fact that higher melting points for nicotinic acid have also been reported, it was thought that our values might be low because of decomposition during the half-hour heating time. To test this possibility, the oil bath was heated to 235° C. before placing the capillary in it and the total time required to take the melt was only 5 minutes. Values of 236.2° and 236.6° C. were obtained on sample *D* for the middle and end of melting, indicating that decomposition is probably not a significant factor.

The reason for the higher values reported is most likely due to too rapid heating during melting or to

the use of a too large capillary, or an air bath rather than an oil bath. Heating sample *D* in the oil bath at a rate of 2° per minute gave values of 236.4° and 237.1° C. for the middle and end of melt, about 1/2° too high. The use of an electrically heated air bath (5) gave values in agreement with the oil bath only when the rate of heating did not exceed 1/2° per minute. When the rate of heating was 2° per minute, the middle and end of melt were 236.4° and 237.8° C., the latter figure being more than a degree too high. When the size of the capillary was increased to a diameter of 1.2 mm., filled to a depth of 7 mm. (instead of 3 mm.) and it was heated in the air bath at 2° per minute, values of 237.2° and 239.2° C. were obtained for the middle and end of melting, the latter figure being 2.5° too high. Nicotinic acid seems to be a substance either of very low heat conductivity or very high specific heat, or possibly it combines both properties. In any event, a heating rate not in excess of 1/2° per minute is needed to obtain the correct melting point.

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SUMMARY

1. The melting points of various commercial and purified samples of nicotinic acid have been determined.

2. The true melting point of nicotinic acid is probably between 235.5° and 236.6° C.

3. In determining the melting point of nicotinic acid, care must be taken to heat not faster than 1/2° per minute or high values will be obtained.

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