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Optical Properties and Preliminary X-ray Investigation of Nicotinic Acid and Nicotinamide

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The optical properties, lattice dimensions and space groups of nicotinic acid, of nicotinamide, and of nicotinamide crystallized from ethylene glycol have been determined and the results obtained are compared with published data. Nicotinamide crystallized from ethylene glycol appears to be a compound of two molecules of nicotinamide with one molecule of glycol as solvent of crystallization.

On the basis of these measurements probable orientations of the molecules in the crystal lattices have been postulated.

This work on the crystal structures of nicotinic acid and of nicotinamide was undertaken as part of a programme of physico-chemical research on the vitamins. The present communication is concerned with the optical properties and X-ray crystallography of these substances. Keenan (1943) has reported some optical properties of both nicotinic acid and nicotinamide, and the results given here are in agreement with his published data. However, McCrone & Cook (1947) have published a more extensive survey of the optical properties of nicotinamide, and it has not been found possible to reproduce their results, or to derive their results from their published data. The crystals of nicotinamide on which McCrone & Cook made their optical determinations were grown from a solution of nicotinamide in ethylene glycol on a microscope slide, and were stated by them to be the common stable form of the amide which is obtained by crystallization of the amide from most common organic solvents. It was found here that, using redistilled ethylene glycol as solvent, a different form of crystal was obtained from that which crystallizes from other common solvents. The optical properties and crystallographic data for both forms are given below.

Morphological and optical properties

Nicotinic acid crystallized from water, industrial spirit, or 1 : 1 mixtures of water, and industrial spirit, appeared either as flat colourless monoclinic plates with {010} as the predominant form, and exhibiting a characteristic edge angle of 114°, or as small rods as noted by Keenan. All crystals were found to be twinned either about the *c* axis or across the 100 plane to a greater or lesser degree, and exhibited a fibrous structure. Examination by means of the polarizing microscope gave the results shown in Table 1.

Nicotinamide crystallized from redistilled ethylene glycol, or from mixtures of ethylene glycol and water containing less than 25 % of water, appeared as monoclinic crystals of prismatic habit, elongated parallel to the *c* axis and showing {110} as the predominant form. When freshly grown the crystals had a silky appearance, but became covered with a white powder on standing in moist air for a few hours. All crystals were found to be twinned either about the *c* axis or across the 100 plane.

Nicotinamide crystallized from water, common organic solvents such as acetone, benzene, glycerol, and from mixtures of water and ethylene glycol containing more than 50 % of water, appeared as lath-shaped monoclinic crystals, elongated parallel to the *c* axis and exhibiting {010} as the predominant form, with a characteristic edge angle of 99° (Table 2).

X-ray data

X-ray Debye–Scherrer, oscillation and Weissenberg photographs (using Cu $K\alpha$ Ni-filtered radiation,

Table 1. *The optical properties of nicotinic acid for sodium light*

	Present work	Keenan's results
n_1	$1{\cdot}424 \pm 0{\cdot}002$	$1{\cdot}428 \pm 0{\cdot}003$
n_2	$1{\cdot}717 \pm 0{\cdot}005$	Indeterminate
n_3	$> 1{\cdot}75 (\sim 1{\cdot}79)$	$> 1{\cdot}734$
Extinction	Both straight and inclined. The maximum extinction angle observed was $13\frac{1}{2}°$	Parallel, although the substance showed many rod-like fragments which did not extinguish sharply
Acute bisectrix	$= X_1$ in a direction $13\frac{1}{2}°$ from the *c* axis in the obtuse angle β	—
Optic plane	Optic plane and X_3 normal to (010)	—
Optic axial angle	$2V_1 = 46°$	—
Optic sign	Negative	—
Maximum birefringence	$> 0{\cdot}32$	—
Monoclinic angle β	114°	—

Table 2. *The optical properties of nicotinamide for sodium light*

	Keenan's results	Nicotinamide crystallized from common solvents	Nicotinamide crystallized from ethylene glycol	McCrone & Cook's results
n_1	$1{\cdot}485 \pm 0{\cdot}002$	$1{\cdot}466 \pm 0{\cdot}003$	$1{\cdot}449 \pm 0{\cdot}005$	$1{\cdot}445 \pm 0{\cdot}002$
n_2	Indeterminate	1·74	$1{\cdot}685 \pm 0{\cdot}005$	$1{\cdot}683 \pm 0{\cdot}002$
n_3	> 1·734	> 1·75 (~ 1·77)	$1{\cdot}694 \pm 0{\cdot}003$	$1{\cdot}711 \pm 0{\cdot}002$
Extinction	Parallel and inclined	Straight and inclined. The maximum extinction angle observed was 23½°	Straight and inclined. The maximum extinction angle observed was 18°	The maximum extinction angle was 25°
Acute bisectrix	—	$= X_1$ in a direction making an angle 23½° with the c axis in the acute angle β	$= X_1$ in a direction making an angle of 18° with the c axis, probably in the obtuse angle β	$= X_1$ in a direction inclined at 25° to the c axis in the acute angle β
Optic plane	—	(010)	Optic plane and X_3 normal to (010)	(010)
Optic axial angle	—	$2V_1 = 32°$	$2V_1 = 23°$	$2V_1 = 29°$
Optic sign	—	Negative	Negative	Negative
Maximum birefringence	—	~ 0·3	~ 0·25	0·266
Monoclinic angle β	—	99°	Not measured optically owing to crystal habit	107°

Table 3. *Single-crystal data*

	Nicotinic acid	Nicotinamide	Nicotinamide crystallized from ethylene glycol
Twinning	All crystals were twinned either about the c axis or across (100)	—	All crystals were twinned either about the c axis, or across (100)
a (A.)	$7{\cdot}175 \pm 0{\cdot}002$	$9{\cdot}435 \pm 0{\cdot}001$	$7{\cdot}16 \pm 0{\cdot}04$
b (A.)	$11{\cdot}682 \pm 0{\cdot}002$	$15{\cdot}65 \pm 0{\cdot}01$	$15{\cdot}6 \pm 0{\cdot}08$
c (A.)	$7{\cdot}220 \pm 0{\cdot}002$	$3{\cdot}974 \pm 0{\cdot}001$	$7{\cdot}58 \pm 0{\cdot}04$
β	113° 23′ ± 3′	99° 8′ ± 5′	116°
Space group	$P2_1/c$	$P2_1/a$	$P2_1/c$
No. of molecules per unit cell	4	4	4 (assumed)
Density (calc.) (g.cm.$^{-3}$)	$1{\cdot}472 \pm 0{\cdot}001$	$1{\cdot}400 \pm 0{\cdot}001$	—
(obs.) (g.cm.$^{-3}$)	$1{\cdot}473 \pm 0{\cdot}002$	$1{\cdot}400 \pm 0{\cdot}002$	1·346
Molecular weight	—	—	154 ± 3
Molecular weight of 1 molecule of nicotinamide + ½ molecule of ethylene glycol	—	—	153

Table 4. *Debye–Scherrer patterns*

Nicotinic acid				Nicotinamide				Nicotinamide crystallized from ethylene glycol			
hkl	Intensity	$d_{obs.}$ (A.)	$d_{calc.}$ (A.)	*hkl*	Intensity	$d_{obs.}$ (A.)	$d_{calc.}$ (A.)	*hkl*	Intensity	$d_{obs.}$ (A.)	$d_{calc.}$ (A.)
110	10	5·740	5·736	110	< 1	7·932	8·006	100	2½	6·427	6·43
120	5	4·370	4·369	120	10	6·006	5·993	110	5½	5·937	5·94
$\bar{1}21$	3	4·191	4·190	130	1	4·547	4·553	120	8	4·963	4·96
111	1	3·724	3·744	220	2	3·998	4·003	031	3	4·127	4·13
$\bar{1}02$	6	3·590	3·586	011	3	3·809	3·806	$\bar{1}31$	3	3·998	4·00
$\bar{1}12$	6	3·431	3·428	140	< 1	3·610	3·608	$\bar{1}02$	2	3·765	3·77
002	9	3·311	3·314	021	4	3·508	3·507	$\bar{1}12$	7	3·659	3·66
012	5	3·187	3·188	$\bar{1}21$	7	3·449	3·448	002	10	3·399	3·40
$\bar{1}22$	1	3·055	3·056	111	< 1	3·346	3·347	$\bar{1}22$			3·39
022	1	2·888	2·882	$\bar{2}01$	8	3·265	3·267	012	3½	3·321	3·32
131	1	2·766	2·774		1	3·138			< 1	3·236	
$\bar{1}41$	2	2·629	2·627		< 1	3·001			< 1	3·179	
	1	2·512			1	2·969			1½	3·115	
	2	2·349			< 1	2·870			< 1	3·044	
	1	2·296			2	2·749			< 1	2·956	
	1	2·257			1	2·668			2	2·846	
	2	2·190			< 1	2·610			< 1	2·769	
	1	2·148			< 1	2·583			< 1	2·604	
	1	2·008			< 1	2·513			< 1	2·559	
	etc.				1	2·433			2½	2·479	
					1	2·328			1	2·407	
					< 1	2·276			< 1	2·297	
					< 1	2·238			< 1	2·199	
					< 1	2·192			< 1	2·132	
					< 1	2·175			etc.		
					< 1	2·082					
					< 1	2·036					
					etc.						

$\lambda(K\alpha)=1{\cdot}5418$ A., $\lambda(K\alpha_1)=1{\cdot}54050$ A., $\lambda(K\alpha_2)=1{\cdot}54434$ A.) were taken on the three types of crystals described above, and the densities were determined by a flotation method in mixtures of methylene iodide and xylene, and of carbon tetrachloride and benzene. The observations are recorded in Tables 3 and 4.

Discussion

(*a*) *Comparison with published data*

The crystals obtained from a solution of nicotinamide in redistilled ethylene glycol are considered to consist of a compound of nicotinamide with ethylene glycol of crystallization. The X-ray data agree with the composition 4 molecules of nicotinamide and 2 molecules of ethylene glycol per unit cell.

There are serious discrepancies between the results now presented for nicotinamide and those published by McCrone & Cook. These workers made optical and crystallographic but not X-ray examinations 'on crystals from ethylene glycol on a microscope slide'. Examination of Table 2 shows that McCrone & Cook's crystals were not those of the form which crystallizes from common solvents. This is in direct contradiction to the statement made in their publication. The fact that McCrone & Cook's value for the density ($1{\cdot}401 \pm 0{\cdot}002$ g.cm.$^{-3}$) agrees with that given here for nicotinamide is explained if their determination was made using, not the crystals from glycol, but the original supply of nicotinamide.

There is considerable agreement between McCrone & Cook's optical data for 'nicotinamide' and that now presented for the compound with glycol of crystallization, and the general appearance of the crystals under the microscope is very similar in the two cases. Moreover, by using McCrone & Cook's value for the monoclinic angle β and certain of our X-ray measurements, it has been found possible to derive a value for the axial ratio $a:b$ for the compound with glycol of crystallization, which is fairly close to that given by McCrone & Cook for their crystals.

On the other hand, there is no apparent agreement between the $b:c$ axial ratios in the two cases, nor can the difference in extinction angles and positions of the optic planes be explained. It is therefore possible that McCrone & Cook's crystals from ethylene glycol consisted of a substance which is neither nicotinamide in the form which crystallizes from common solvents, nor nicotinamide with ethylene glycol of crystallization, but some other form of nicotinamide. Repeated efforts made here, however, to obtain such a form by crystallization from a solution of nicotinamide in ethylene glycol have failed. The single compound, which is considered to be nicotinamide with ethylene glycol of crystallization, has been obtained in every case.

(*b*) *Possible molecular orientations*

As the pyridine ring is planar, the large negative birefringence and the value of the extinction angle of the nicotinic acid crystals suggest that the molecules all lie roughly with the pyridine rings in a plane making an angle of $\sim 10°$ in the obtuse angle β with the $a\,b$ plane. This plane is almost parallel to $\bar{1}06$, which makes an angle of $9\frac{1}{2}°$ with the $a\,b$ plane, in the obtuse angle β. Further, it was observed that on the $h0l$ Weissenberg photograph, the $\bar{1}06$ reflexion is strong. This reflexion, for which the Bragg angle is 41°, was not observed on the Debye–Scherrer photograph because of the geometrical factors peculiar to the Debye–Scherrer method.

As the compound with glycol of crystallization shows large negative birefringence, and on the assumption that the acute bisectrix lies in the obtuse angle β, it is probable that the nicotinamide molecules lie with the pyridine rings in the 002 planes, which give rise to a very strong X-ray reflexion observed on the $h0l$ Weissenberg photograph. The two molecules of ethylene glycol present in the unit cell must lie at equivalent centres of symmetry.

The optical properties of nicotinamide crystallized from common solvents suggest that the nicotinamide molecules lie with the pyridine rings in the $\bar{4}03$ planes. The $\bar{4}03$ reflexion on the $h0l$ Weissenberg photograph is observed to be strong.

In order to establish the structures of these crystalline materials, further work is in progress.

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