

THE OPTICAL CRYSTALLOGRAPHIC PROPERTIES OF CRYSTALS FORMED WITH NITRIC ACID FROM PETHIDINE, NICOTINAMIDE AND CINCHOPHEN

BY ALF WICKSTRØM

From the Department of Pharmaceutical Chemistry, Institute of Pharmacy, University of Oslo

Received March 31, 1950

THE author has on an earlier occasion reported that pethidine forms with nitric acid characteristic crystals which may be useful for the micro-identification of this substance¹. As pethidine is in many countries subject to the restrictions of the Opium Convention, its micro-identification may have significance. In the opinion of Professor B. Samdahl optical crystallography is useful in the analysis of crystalline pharmaceutical substances, and for this reason he urged me to examine the crystalline compound of pethidine and nitric acid by means of the polarising microscope and ascertain its optical data.

The optical characters have also been observed in respect of crystals obtained with nitric acid from other substances listed in the Scandinavian Pharmacopœias. Among these substances the following have been stated in the literature as giving colourless crystals with nitric acid: pethidine, nicotinamide and cinchophen. Among substances not listed in the Scandinavian Pharmacopœias, sulphaguanidine forms a crystalline complex with nitric acid, the optical characters of which have been examined by G. L. Keenan². The purpose of this paper is to report the microscopical characters in polarised light of the crystals formed with nitric acid from the other three substances.

The refractive indices were determined for yellow light by the immersion method (all ± 0.002). The principal indices were determined statistically in contused material in order to ensure that the particles lay in random formation. Significant intermediate refractive indices, observed in a preferred orientation of the crystals, are reported when they may be useful in the identification of the substance.

PETHIDINE

The crystals are precipitated on a microscope slide from a drop of an aqueous solution of pethidine hydrochloride (5 to 10 per cent.) with 5 M nitric acid. Solid pethidine may also be added to a drop of nitric acid.

Crystal habit. Lance-shaped crystals of variable length. Sometimes small crystals of rhombic silhouette.

Characters shown in parallel polarised light. (Crossed Nicols). Usually no interference colours, some larger crystals having low order colours. Extinction usually unsymmetrical. Elongation negative. The crystals of rhombic silhouette have symmetrical extinction: $\frac{1}{2}(43^\circ \pm 1)$.

Characters shown in convergent polarised light. (Crossed Nicols). An off-centred biaxial optic axis figure is commonly found. Optic sign: positive.

Refractive indices. $\alpha = 1.572$, $\gamma = 1.590$, $1.575 < \beta < 1.582$.

Distinctive optical characters. $n_i = 1.575$ frequently found lengthwise, and $n_i = 1.585$ less frequently found crosswise, are useful in the identification of the substance.

System. Monoclinic.

PETHIDINE, NICOTINAMIDE AND CINCHOPHEN

NICOTINAMIDE

2 ml. of an aqueous solution of nicotinamide (5 per cent.) is mixed with 1 ml. of 5 M nitric acid (Swedish Pharmacopœia 1946). The precipitation is performed on a microscope slide with a drop of each reagent. Solid nicotinamide may be added or a more concentrated solution may be used.

Crystal habit. Elongated rods with rectangular, parallelogramatic or irregular silhouette. They occur isolated or linked together at one of their elongated planes.

Characters shown in parallel polarised light. (Crossed Nicols). White of higher order commonly shown. Some rods have brilliant interference colours and positive elongation. Extinction usually oblique. Extinction dispersion sometimes observed. Some of the rods with brilliant interference colours have parallel extinction. The rods linked together prove to be a characteristic polysynthetic twin formation with extinction angle $5^\circ \pm 1$.

Characters shown in convergent polarised light. (Crossed Nicols). On the rods having parallel extinction the interference figure of an acute positive bisectrix is always observed.

Refractive indices. $\alpha = 1.410$, β not determined, $1.730 < \gamma < 1.741$.

Distinctive optical characters. γ is frequently observed and may be useful in the identification of the substance. The polysynthetic twin formation is also characteristic.

System. Monoclinic. α parallels the β crystallographic axis. $2V = 40$ to 60° . Plane 010 well developed.

CINCHOPHEN

A few mg. of the substance are dissolved in 1 drop of 10 per cent. ammonia on a microscope slide and 1 or 2 drops of 5 M nitric acid are added, Wagenaar³.

Crystal habit. Small needles occurring isolated or arranged in rosettes.

Characters shown in parallel polarised light. (Crossed Nicols). Brilliant interference colours. Extinction parallel or nearly parallel. Elongation positive.

In convergent polarised light no interference figures can be obtained on the small needles. The particles in contused material will be extremely small and the principal refractive indices cannot be exactly determined.

Distinctive optical characters. $1.730 < \gamma < 1.741$ is frequently observed lengthwise. Crosswise the index 1.492 is frequently found.

SUMMARY

Optical data are presented for the crystals obtained by the micro-chemical reaction with nitric acid from pethidine, nicotinamide and cinchophen. The results are of value in the rapid identification of these substances.

REFERENCES

1. Wickström, *Med. Norsk Farm. Selska.*, 1946, **8**, 212.
2. Keenan, *J. Amer. Pharm. Ass. Sci. Ed.*, 1948, **37**, 202.
3. Wagenaar, *Pharm. Weekbl.*, 1934, **71**, 1100.