

97. *The Veratrine Alkaloids. Part III. The Preparation of Cevanthrol, and the X-Ray Crystallographic Examination of Cevanthrol and Cevanthridine.*

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THE selenium dehydrogenation of cevine to a crystalline base $C_{23}H_{25}N$ (cevanthridine) was described in Part II (J., 1935, 124). By modifying the method of isolation, we have now obtained a second dehydrogenation product, $C_{17}H_{16}O$, which we have named *cevanthrol*, in just under 5% yield. Its oxygen atom is phenolic, since it dissolves in hot alkali and forms an *acetyl* derivative. The related hydrocarbon is therefore $C_{17}H_{16}$, which corresponds to a substituted phenanthrene, $C_{14}H_{10} + C_3H_6$.

In order to gain an insight into the structure of this substance and of cevanthridine we have made a preliminary X-ray examination of crystals of both of them. Table I gives the results obtained together with the approximate orientation of the optic axes in the crystals. The cell dimensions are correct to about 2%.

TABLE I.

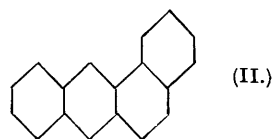
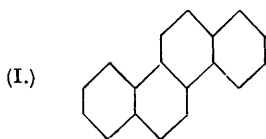
Substance.	<i>a.</i>	<i>b.</i>	<i>c.</i>	—	Space group.	No. of mols. in unit cell.	No. in asym-metric unit.	Density calc.
Cevanthrol.....	16.7	7.0	23.8	107°	P2 ₁ /a	8	2	1.17
	<i>α</i>	<i>β</i>	<i>γ</i>					
Cevanthridine	6.8	15.55	17.35	90°	P2 ₁ /a?	4	1	1.13
	<i>β</i>	<i>α</i>	<i>γ</i>					

The crystal unit cell of cevanthrol contains eight molecules, twice as many as that required by the symmetry, and it is therefore impossible to determine with certainty their orientation in the unit cell. But the very marked weakening of the odd orders of the *c* plane indicates the presence of a double layer of molecules placed lengthwise along *c* (*γ*) such as is found in the fatty acids and alcohols. From this we may deduce approximately the orientations and dimensions of the molecules as length probably about 12 Å. along *c*/2 (*γ*), width 7 Å. along *b* (*β*), and thickness 4 Å. in the *a* plane, $a \sin \beta/4$ (*α*). These dimensions agree closely with those found for other alkylphenanthrene derivatives in which the 9- and 10-positions are left unsubstituted (Bernal and Crowfoot, J., 1935, 93). Further, it is almost certain that the double layer is caused by the association of molecules together by bonds between the hydroxyl groups (Bernal and Megaw, *Proc. Roy. Soc.*, 1935, 151, 384) such as occurs, for example, in the sterols (Bernal, *Nature*, 1932, 129, 277) and in the more completely investigated structure of resorcinol (Robertson, *Nature*, 1935, 136, 755). This permits us to deduce that the hydroxyl group in cevanthrol is most probably placed at one end of the molecule, preferably in position 3.

The crystallography of cevanthridine presents certain problems, since, although the halvings present were those of the monoclinic space group P2₁/a, no departure could be observed from orthorhombic symmetry. The photographs were, however, not very good, since the crystals grown from the melt were very imperfectly formed. As in the case of the aromatic hydrocarbons obtained in a similar way from the sterols, it is probable that these crystals consist of multiple twins and therefore can simulate orthorhombic symmetry. It is also just possible that the *c* dimension is double that recorded, since the photographs about [001] gave such blurred reflections that it was difficult to distinguish the true identity period. The crystal structure would then be very closely similar to that of the metastable modification of the hydrocarbon $C_{26}H_{26}$ from ergosterol, to which in any case it appears to have some relations.

The doubt as to the actual symmetry of the crystals does not affect the determination of the approximate arrangement of the molecules in the cell, since this is clearly indicated by the optic orientation and the marked intensity variations of the reflections, particularly the exceedingly strong fourth order of the *b* plane. From these data we may deduce the presence of molecules of dimensions approximately $17 \times 6.8 \times 3.8$ Å. arranged with their lengths along *c* (*γ*), widths in *a* (*β*), and thickness four times over in *b* (*α*). This agrees further with the marked *b* cleavage.

The most plausible chemical structure for cevanthridine in agreement with these dimensions would appear to be one based on a condensed ring system of either type (I) or (II).



We reserve further discussion of these substances until more is known about their chemistry; but we wish to emphasise the mildness of the conditions employed in the dehydrogenation. Ruzicka and Peyer (*Helv. Chim. Acta*, 1935, **18**, 676) have shown that both α - and β -methylhydrindene are stable when heated with selenium below 400°, but at 450° ring enlargement to naphthalene occurs. Since the dehydrogenation of cevine was carried out at 320—330°, it seems likely that the ring systems of cevanthrol and cevanthridine largely exist ready-formed in cevine.

EXPERIMENTAL.

Cevanthrol.—Hydrated cevine (15 g.) and selenium (30 g.) were heated together in a 50 c.c. flask under the conditions previously described (*loc. cit.*). After cooling, ether was added, and the flask kept for 1—2 hours with occasional shaking. The ethereal extract was decanted, and the residue shaken several times with small quantities of fresh ether. The united extracts were filtered, and shaken first with dilute hydrochloric acid, whereby cevanthridine was removed as the insoluble hydrochloride, and then several times with aqueous alkali. The alkaline extracts were brilliant blue-green and gave no crystalline material on acidification. Finally, the ethereal solution was washed with water, dried, and evaporated, and the residue crystallised from benzene, giving cevanthrol in almost colourless crystals, m. p. 190—193°. By heating the selenium residues for a second period of 15 hours, and working up as before, further small amounts of both base and phenol were obtained. The final yield was 1.3—1.4 g. of cevanthridine picrate and 0.27—0.29 g. of cevanthrol. The regulus remaining after the second heating was powdered and extracted, but no crystalline material could be isolated.

Cevanthrol, after repeated crystallisation from benzene, formed rosettes of colourless plates, m. p. 197—198° (Found: C, 86.5; H, 6.7. $C_{17}H_{16}O$ requires C, 86.4; H, 6.8%). It was insoluble in cold aqueous alkali, but dissolved on heating.

The *acetate* was prepared by boiling a solution of the phenol (65 mg.) in acetic anhydride (1.5 c.c.) for 3 hours, and then adding water (0.7 c.c.) gradually to the hot solution. On scratching, the acetyl compound separated; it was recrystallised twice from acetic acid, forming thin diamond-shaped plates, m. p. 138—139° (Found: C, 82.0; H, 6.4. $C_{19}H_{18}O$ requires C, 82.0; H, 6.5%).

Morphology of Cevanthrol.—The small leaf-shaped plates of cevanthrol were elongated along *a* and showed only the (001) face. The plane of the optic axes is (010) with γ inclined at about 20° to the normal to the *c* plane. The birefringence is medium, positive and the optic axial angle fairly large.

Oscillation photographs were taken about the *a* axis.

Morphology of Cevanthridine.—Cevanthridine was obtained from solution as very minute, thin plates. Recrystallisation for X-ray work was effected by melting and recoiling a small sample on a cover-slip under a heat gradient produced by means of a hot wire. The substance then crystallised in sheets on (001), which showed a very marked *b* cleavage. This made it easy to break off needle-shaped fragments for further measurement. Through the *c* face a biaxial figure was visible which showed a very close approximation to orthorhombic symmetry, with γ normal or nearly normal to (001), α along *b*, β along *a*. The birefringence was high, positive and the optic axial angle medium.

Oscillation photographs were taken about all three axes.

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