

XC.—*The Non-resolution of Racemic Tetrahydropapaverine by Tartaric Acid.*

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ON the publication of our note (Proc., 1898, 122) announcing the racemic nature of tetrahydropapaverine and its resolution into optically active components, G. Goldschmiedt, who first prepared this base (*Monats.*, 1886, 7, 485), published a paper (*Monats.*, 1898, 19, 321) in which he stated that he has been occupied for several years on the same problem, and that, although he did not succeed in resolving the racemic base, he had prepared its dextrotartrate, determining its composition, and establishing many points of interest concerning the salt.

During the course of our work (see preceding paper), we prepared and carefully examined this salt, but the appearance of Goldschmiedt's paper renders the publication of much of our work on the subject superfluous. There are, however, several points about the compound which make it one of great interest.

Goldschmiedt states that racemic tetrahydropapaverine forms a single

salt with dextrotartaric acid of the composition $(C_{20}H_{25}NO_4)_2 \cdot C_4H_6O_6 + 17H_2O$, and attributes his failure to resolve the base to the fact that this compound is a neutral salt, and that no acid salt could be prepared. We also were unable to prepare an acid dextrotartrate from the racemic base, and obtained the neutral salt which has the composition he assigned to it.

On allowing its hot aqueous solution to cool slowly, the tartrate crystallises in small, colourless, transparent prisms, which have a brilliant lustre and effloresce on exposure to the air. The crystals, which were examined in order to demonstrate that the salt is not a mixture, belong to the monosymmetric system, the dominant form being $p \{110\}$ (Fig. 1); the next largest form observed is $q \{011\}$ and the faces of this form give the best reflections of any on the crystals. The two pinacoids $a \{100\}$ and $b \{010\}$ are rarely observed and are always very small. It is difficult to obtain trustworthy measurements of these crystals, inasmuch as the faces are all rather distorted.

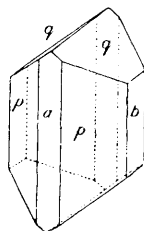
Crystalline System.—Monosymmetric.

$$a : b : c = 1.1464 : 1 : 0.7932$$

$$\beta = 82^\circ 30'$$

Forms observed.— $a \{100\}$, $b \{010\}$, $p \{110\}$, and $q \{011\}$.

FIG. 1.



The following angular measurements were obtained.

Angle.	Number of measurements.	Limits.	Mean observed.	Calculated.
$ap = 100 : 110$	26	$47^\circ 38' - 49^\circ 41'$	$48^\circ 27'$	$48^\circ 39.5'$
$pp = 110 : \bar{1}10$	42	$81^\circ 56' - 83^\circ 39'$	$82^\circ 41'$	—
$pp = 110 : 1\bar{1}0$	37	$96^\circ 12' - 97^\circ 1'$	$97^\circ 10'$	$97^\circ 19'$
$bp = 010 : 110$	16	$40^\circ 22' - 42^\circ 19'$	$41^\circ 12'$	$41^\circ 20.5'$
$bq = 010 : 011$	13	$50^\circ 48' - 52^\circ 35'$	$51^\circ 38'$	$51^\circ 49'$
$qq = 011 : 0\bar{1}1$	48	$75^\circ 14' - 77^\circ 36'$	$76^\circ 22'$	—
$qq = 011 : 01\bar{1}$	29	$102^\circ 40' - 104^\circ 52'$	$103^\circ 47'$	$103^\circ 38'$
$pq = 110 : 01\bar{1}$	24	$65^\circ 17' - 67^\circ 58'$	$66^\circ 39'$	—
$pq = 110 : 011$	9	$56^\circ 31' - 59^\circ 0'$	$57^\circ 14'$	$57^\circ 52'$

The crystals are very brittle and show no definite cleavage. On examination through $p\{110\}$, the extinction is seen to be very oblique to the long edge of the crystals, and one optic axis of a biaxial interference figure is observed emerging in the field.

Landolt (*Ber.*, 1873, 6, 1077) showed that the metallic tartrates have nearly the same molecular rotation, namely, $[M]_D = +58.1^\circ$ to $+64.6^\circ$, in fairly dilute aqueous solution, so that the molecular rotation of the salt is nearly independent of the base which it contains. These results have been extended by Oudemans (*Annalen*, 1879, 197, 48, 66; 1881, 209, 38), Tykociner (*Rec. Trav. Chim.*, 1882, 1, 144) and others. It was therefore to be expected that the molecular rotation of racemic tetrahydropapaverine dextrotartrate would also have a value of about $+60^\circ$; the sparing solubility of the salt renders the accurate determination of the molecular rotation difficult.

A solution of 0.9539 gram of the salt dried at 100° , made up to 100 c.c. with water, gave $\alpha_D = +0^\circ 17'$ in a 400 mm. tube, whence $[\alpha]_D = +7.43^\circ$ and $[M]_D = +63.4^\circ$.

A solution of 1.0069 grams of salt dried at 100° , made up to 100 c.c. with water, gave $[\alpha]_D = +0^\circ 18'$ in a 400 mm. tube, whence $[\alpha]_D = +7.45^\circ$ and $[M]_D = +63.6^\circ$.

A solution containing 1.1397 grams in 100 c.c. crystallised on cooling.

The mean values are $[\alpha]_D = +7.44^\circ$ and $[M]_D = +63.5^\circ$, so that the molecular rotation is, within the limits of experimental error, of the same magnitude as those of the metallic tartrates.

After adding excess of ammonium hydroxide to the hot solution of the salt and allowing to cool, the base separates as minute, glistening needles which, after drying at 110° , melt at $200\text{--}201^\circ$; a polarimetric examination of a chloroform solution containing 2 grams per 25 c.c. in a 200 mm. tube showed the base to be racemic tetrahydropapaverine.

Since we have previously demonstrated the racemic nature of inactive tetrahydropapaverine, it is obvious that the neutral tartrate contains a molecule each of the dextro- and lævo-base to each molecule of tartaric acid. The compound is therefore one of the kind which Ladenburg has recently discovered (*Ber.*, 1898, 31, 524) and described as "halbrcemisch," a term which may be translated as "hemiracemic." The failure to resolve racemic tetrahydropapaverine by crystallisation with tartaric acid must be attributed to the occurrence of partial racemism, and not to the fact that the base does not yield an acid tartrate. There seems no *à priori* reason why a racemic base should not be resolvable by crystallising its neutral salt with an optically active acid as well as by crystallising its acid salt; in fact, we resolved the base by means of its neutral salts with dextro- α -bromocamphor-sulphonic acid.

Up to the present, the following partially racemic compounds have

been described namely, quinine racemic pyrotartrate (Ladenburg, *Ber.*, 1898, 31, 524, 937), and strychnine racemate (Ladenburg and Doctor, *Ber.*, 1898, 31, 1969).

Racemic tetrahydropapaverine dextrotartrate is thus the first partially racemic substance containing an externally compensated base which has been examined; it should, however, be mentioned that Ladenburg notes his inability (*Ber.*, 1894, 27, 75; 1898, 31, 524) to resolve inactive β -pipercoline by means of its bitartrate at the temperature of the water bath, owing apparently to the occurrence of partial racemism.

It must be concluded that if an inactive substance cannot be resolved into optically active compounds by crystallising its salts with an optically active base or acid, it is nevertheless still possible that the inactive compound is an externally compensated substance.

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