XX.—*The Resolution of dl-Methylhydrindamine. Isomeric Salts of d- and l-Methylhydrindamines with d-Chlorocamphorsulphonic Acid.*

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IN a recent communication (Tattersall and Kipping, *Trans.*, 1903, **83**, 918), a method was described by which *dl*-methylhydrindamine could be resolved into its enantiomorphously related components by the use of *d*-bromocamphorsulphonic acid. As the yield of these salts of the *d*- and *l*-bases was always small compared with the quantity of original material taken, and also varied considerably with the conditions of the experiment, the author, at Dr. Kipping's suggestion, attempted to find a more satisfactory process for the resolution of the *dl*-base.

Experiments then showed that *d*-tartaric acid is a more suitable agent with which to effect the resolution. When a solution of this acid is added to *dl*-methylhydrindamine in sufficient quantity to form the hydrogen tartrate and the product fractionated from water at the ordinary temperature, an excellent separation of the *d*- and *l*-bases is effected. The most sparingly soluble fractions, which contain the hydrogen tartrate of the *d*-base in a pure condition, amount to about one-third of the whole material.

The purification of the bases was carried out by converting the first fractions, containing chiefly the *d*-base, and the last fractions (the remaining two-thirds) into the *d*-bromocamphorsulphonates separately, and finally fractionating the products by crystallising from water.

The production of isomeric salts by the combination of *d*- and *l*-methylhydrindamines with *d*-bromocamphorsulphonic acid has been already described (Tattersall and Kipping, *loc. cit.*), and in this paper an account is given of similar experiments made with *d*-chlorocamphorsulphonic acid and the same bases.

The salt of each base, prepared from very carefully purified materials, was subjected to repeated fractional crystallisation and the final fractions examined. In both cases, the melting points of successive fractions were found to decrease from the first to the last, this behaviour corresponding with that observed in the case of the bromocamphorsulphonates. An important point of difference between the chlorocamphorsulphonates and the bromocamphorsulphonates, however, is that in the case of the former acid the specific rotations of the last fractions are higher than those of the first fractions, whereas with the latter acid the reverse is the case. These generalisations are true

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both for aqueous and chloroform solutions. The following table summarises the results obtained:

l-Methylhydrindamine *d*-chlorocamphorsulphonate.

	M. p.	[α] _D .	
		In chloroform.	In water.
First fraction	239°	+ 3.3°	+ 34.2°
Last „	231—233°	8.0	35.8

d-Methylhydrindamine *d*-chlorocamphorsulphonate.

	M. p.	[α] _D .	
		In chloroform.	In water.
First fraction	247°	+ 56°	+ 60°
Last „	225—230°	63	63

These results are similar to those obtained with the hydrindamine *d*-chlorocamphorsulphonates (Kipping, Trans., 1903, 83, 902), but it was not found possible to isolate the isomerides of higher specific rotation.

EXPERIMENTAL.

About 30 grams of purified *dl*-methylhydrindamine *d*-bromocamphorsulphonate, obtained as previously described (Tattersall and Kipping, *loc. cit.*), was decomposed with barium hydroxide and the base distilled in steam. A solution of *d*-tartaric acid was added to the distillate until the latter was just acid, and then a further equal quantity of acid in order that the hydrogen tartrate might be produced. The solution was evaporated and the salt fractionally crystallised. The first deposit on recrystallisation was obtained in vitreous prisms, whilst the mother liquors slowly deposited clusters of small, opaque crystals. When the fractionation had proceeded so far that the first deposit had been twice crystallised, the first two fractions were examined. The first was found to be hydrated and when dried, melted at about 150°; the second was almost anhydrous and melted at 190° (approximately). The fractions were therefore different.

The first fraction, amounting to about one-fourth or one-third of the whole, was decomposed with caustic potash, the base distilled in steam, the distillate neutralised with *d*-bromocamphorsulphonic acid, and the solution evaporated and crystallised, when the salt of *d*-methylhydrindamine was obtained. The sparingly soluble fractions of the hydrogen tartrate therefore contain the *d*-base.

Owing to the difficulty usually experienced in obtaining a pure salt

from the mother liquors, and considering the great ease with which *dl*-methylhydrindamine *d*-bromocamphorsulphonate can be separated from the salt of the *d*- or *l*-base, the last fractions were decomposed with caustic potash, the base distilled in steam and combined with *d*-bromocamphorsulphonic acid. On crystallising, the salt of *l*-methylhydrindamine first separated and the salt of the *dl*-base was found in the mother liquors.

The *d*-base can, obviously, be obtained pure from the first deposits of the hydrogen tartrate, but the purification of the *l*-base was always carried out by converting the last fractions into the *d*-bromocamphorsulphonate.

By this process, about two-thirds of the original *dl*-base can be resolved into its enantiomorphously related components.

d-Methylhydrindamine Hydrogen Tartrate, $C_{10}H_{13}N, C_4H_6O_6, 2H_2O$.—This salt crystallises from water in long, vitreous, hydrated prisms which become opaque on warming in contact with a solution of the salt; it is moderately soluble in alcohol or water, but more sparingly so in the latter solvent than the corresponding salt of the *l*-base, and is practically insoluble in chloroform, ether, ethyl acetate, and light petroleum. The melting point of the dried salt is $153-155^\circ$, being somewhat indefinite owing to slight decomposition.

The water was estimated in air-dried samples by determining the loss of weight at 100° .

2.6761 lost 0.2868. $H_2O = 10.7$.

$C_{10}H_{13}N, C_4H_6O_6, 2H_2O$ requires $H_2O = 10.8$ per cent.

The specific and molecular rotations were determined in aqueous solution with samples of the anhydrous salt, 20 c.c. of solution being used.*

Weight of salt.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.5376	+1.74°	+32.4°	+98.0°
0.5925	1.99	33.6	99.7

As the molecular rotation of *d*-tartaric acid in the metallic hydrogen tartrates is $[M]_D + 42^\circ$, that of the base would be $[M]_D + 57^\circ$, a value which agrees very closely with that ($[M]_D + 60^\circ$) previously determined from an examination of the *d*-bromocamphorsulphonates (Tattersall and Kipping, *loc. cit.*).

l-Methylhydrindamine Hydrogen Tartrate, $C_{10}H_{13}N, C_4H_6O_6$.—This salt crystallises from water in aggregates of small, vitreous, anhydrous prisms, which are readily soluble in water, sparingly so in

* A 200 mm. tube was used in all the polarimetric observations recorded in this paper.

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alcohol, and practically insoluble in chloroform, ethyl acetate, ether, and light petroleum; it melts at 197° with slight decomposition. The specific and molecular rotations were determined in aqueous solution with samples dried at 100°, 20 c.c. of solution being used.

Weight of salt.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.7076	- 0.36°	- 5.0°	- 14.8°
0.6649	0.32	4.8	14.3

In this case, also, the calculated value for the molecular rotation of the *l*-base, namely, $[M]_D - 56.5^\circ$, agrees closely with that previously deduced from the optical examination of the *d*-bromocamphorsulphonates.

l-Methylhydrindamine *d*-Chlorocamphorsulphonate,
 $C_{10}H_{13}N, C_{10}H_{14}OCl \cdot SO_3H$.

This salt was prepared in the usual way, the *l*-methylhydrindamine being carefully purified by the crystallisation of its *d*-bromocamphorsulphonate. The product was subjected to prolonged fractional crystallisation from water and separated into eight fractions. At the conclusion of the fractionation, the melting points of the several fractions were determined, those of the first and last fractions being 239° and 231—233° respectively. The other fractions each melted over a range of 2—3°, the values gradually decreasing from the melting point of the first fraction to that of the last. These fractions all crystallised in anhydrous needles resembling the corresponding salt with *d*-bromocamphorsulphonic acid.

The first and last fractions were dried at 100° and examined polarimetrically in chloroform and aqueous solutions.

First Fraction.

Weight of salt.	Solvent.	Vol. of solution.	α_D	$[\alpha]_D$.	$[M]_D$
I. 0.3496	Chloroform	20 c.c.	+ 0.12°	+ 3.4°	+ 14.0°
II. 0.3351	„	„	0.11	3.28	13.5
I. 0.3496	Water	„	1.19	34.1	140.8
II. 0.3351	„	„	1.15	34.3	141.6

Last Fraction.

I.	0.3294	Chloroform	20 c.c.	+ 0.27°	+ 8.2°	+ 33.8°
II.	0.3327	„	„	0.26	7.8	32.2
I.	0.3294	Water	„	1.18	35.8	147.8
II.	0.3327	„	„	1.19	35.8	147.8

It will be noticed that the specific rotations of the last fraction are higher than those of the first both in chloroform and in aqueous solutions. This conclusively proves that the observed difference in rotation cannot be due to any impurity, although the absence of the latter was independently proved, as in all previous experiments. The existence of isomeric salts is therefore established in this case.

d-Methylhydrindamine, purified by the crystallisation of its bromocamphorsulphonate, was combined with *d*-chlorocamphorsulphonic acid, the product subjected to fractional crystallisation from water, and the melting points of the successive fractions determined. The first fraction melted at 247° and the last at 225—230°.

The intermediate fractions had melting points which, extending over a small range, gradually decreased from the melting point of the first fraction to that of the last. These fractions all separated in anhydrous needles resembling the corresponding bromocamphorsulphonate. The first and last fractions were dried at 100° and examined polarimetrically in chloroform and aqueous solutions.

First Fraction.

Weight of salt.	Solvent.	Vol. of solution	α_D .	$[\alpha]_D$.	$[M]_D$.
I. 0.3912	Chloroform	20 c.c.	+ 2.20°	+ 56.2°	+ 231.1°
II. 0.3953	"	"	2.20	55.7	230.0
I. 0.4049	Water	"	2.44	60.2	248.6
II. 0.4012	"	"	2.41	60.1	248.2

Last Fraction.

I. 0.3696	Chloroform	20 c.c.	+ 2.35°	+ 63.6°	+ 262.6°
II. 0.3917	"	"	2.43	62.2	256.8
I. 0.3696	Water	"	2.34	63.4	261.8
II. 0.3917	"	"	2.44	62.4	257.7

In the foregoing tables, numbers I and II indicate different portions of the same sample of material.

The data show that the specific rotations of the last fraction are higher than those of the first, and for the same reasons as in previous cases, these results establish the existence of isomeric salts.

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