285. *Stereoisomerides of Narcotine and Hydrastine.*

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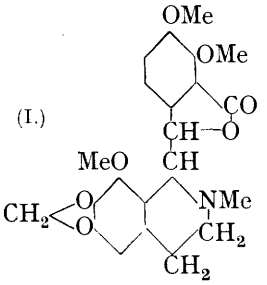
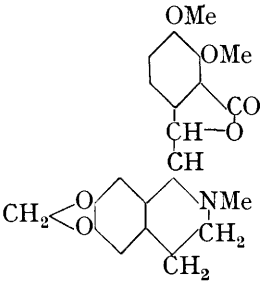
MEMBERS of the phthalide group of *iso*quinoline alkaloids contain two asymmetric carbon atoms in the molecule and hence each should exist in two inactive and four optically active forms. In the narcotine series (I) we are acquainted with *dl*-narcotine or α-gnoscopine



(I.)



(II.)

which on resolution furnishes natural *l*-α-narcotine and its enantiomorph (Perkin and Robinson, J., 1910, **97**, 775), and also with β-gnoscopine (Hope and Robinson, J., 1914, **105**, 2085) obtained from synthetic nitro-β-gnoscopine by eliminating the nitro-group in a series of reactions. This isomeride of α-gnoscopine could not be resolved, but it yielded the α-base on prolonged treatment with hot alcohol.

In the hydrastine (II) series, in addition to natural *l*-hydrastine, there are the synthetic hydrastines-*a* and -*b* (Hope, Pyman, Remfry, and Robinson, J., 1931, 236), the relationships of which have not hitherto been elucidated.

We have now observed that the prolonged action of hot methyl-alcoholic potassium hydroxide on narcotine and hydrastine results in the formation of an equilibrium mixture of the original base and a new optically active isomeride in each case, and thus brings about

partial racemisation or reversible inversion at only one of the asymmetric centres. A similar phenomenon is the epimerisation of aldonic acids in the carbohydrate group under the influence of basic catalysts, and in the present cases the secondary alcoholic and carboxyl groups are separated by an aromatic double bond or system of bonds providing a channel for an electromeric displacement.

On considering these and other analogies, there can be little doubt that the " phthalide " asymmetric carbon atom is the one affected in this process, and the fact that full racemisation occurs to only an inconsiderable extent leads to the corollary that the environment of the " *iso*quinoline " carbon atom is unchanged under these conditions. (Attempts to find an agent capable of specific racemisation of the *iso*quinoline centre were not successful; it seems that reagents which can transpose these groups also attack the phthalide section, and complete racemisation results.) It will be appreciated that the lactone ring must be opened in the hot alkaline solution and that it is really the potassium salt of the hydroxy-acid that undergoes change.

The new l-β-*narcotine* is lævorotatory, and has a considerably lower rotatory power than the naturally occurring *l*-α-narcotine. A small specimen of d-α-narcotine was partly converted into d-β-*narcotine*, and a mixture of *l*-β-narcotine and *d*-β-narcotine furnished β-gnoscopine, identical with the known synthetic base. Thus α- and β-gnoscopine represent the two possible racemates. In confirmation, they are partly interconvertible under the influence of methyl-alcoholic potash.

On the other hand, natural *l*-hydrastine, which for this reason we consider to be *l*-β-hydrastine, yields by partial racemisation an isomeride of higher rotatory power, considered to be *l*-α-hydrastine. Thus naturally occurring hydrastine is believed to differ from naturally occurring narcotine in its stereochemical configuration.

The argument is strengthened by a consideration of the rotatory powers based on a hypothesis of separate contributions by the " *iso*quinoline " and the " phthalide " section, such that these contributions are in the same sense and added together in the α-forms, but are in opposite directions in the β-varieties (internally compensated).

The actual values for $[\alpha]_{\lambda 546}$ in chloroform solution are: *l*-α-narcotine, $-246°$; *l*-α-hydrastine, $-163°$; *l*-β-narcotine, $-101°$; *l*-β-hydrastine, $-68{\cdot}3°$. Whence, on the above-mentioned hypothesis: Contribution of phthalide group: 72·5° narcotine; 47·5° hydrastine. Contribution of *iso*quinoline group: 173·5° narcotine; 115·5° hydrastine. (The allocation of the shares to the phthalide and *iso*quinoline groups is based on the hypothesis that *l*-α-narcotine is *l*-phthalide/*l*-*iso*quinoline and *l*-β-narcotine is *d*-phthalide/*l*-*iso*quinoline.)

The ratio of these contributions is 2·39 for narcotine and 2·43 for hydrastine. The same principle holds roughly for values taken under other conditions, *e.g.*, with the D-line, and no regularity can be brought out on the assumption that natural hydrastine is *l*-α-hydrastine stereochemically parallel to *l*-α-narcotine.

An interesting consequence of the acceptance of this line of argument is that the methoxyl group constituting the difference between hydrastine and narcotine has a constitutive influence on the rotatory power of the molecule as a whole and not merely of that section of it in which it is found (the *iso*quinoline section).

As we are not in possession of specimens of *d*-α-hydrastine or *d*-β-hydrastine, it is very difficult to state with certainty the relation of the synthetic inactive bases, hydrastine-*a* and -*b* to the two *l*-hydrastines, α and β. The behaviour of the isomeric hydrastines towards racemising agents suggests, however, that hydrastine-*a* is *dl*-β-hydrastine and hydrastine-*b* is *dl*-α-hydrastine. Thus, the racemisation of natural *l*-β-hydrastine and of *l*-α-hydrastine by means of aqueous alcohol under pressure gives respectively hydrastine-*a* and -*b*. Furthermore, the equilibrium in the treatment of *l*-β-hydrastine or *l*-α-hydrastine with methyl-alcoholic potash favours the latter base, and hydrastine-*a* is largely converted into hydrastine-*b* under similar conditions.

Nevertheless, the yields obtained in the prolonged racemisation processes are low owing to the formation of by-products, and further investigations are required in order to clear up these remaining doubtful issues. It may be noted that the assumption that hydrastine-*a* is *dl*-β-hydrastine makes the nitrohydrastine series stereochemically analogous to the

nitrognoscopine series, and indeed, these substances run parallel in their physical properties. The clearest example is the similarity of amino-β-gnoscopine and aminohydrastine-*a* in m. p., solubility relations, and crystalline habit.

Taking into consideration the fact that α- but not β-gnoscopine, may be resolved, we conclude that the completion of the synthesis of the naturally occurring hydrastine will probably involve the resolution of hydrastine-*b* and this should afford *l*-α-hydrastine. The final stage, the epimerisation of *l*-α-hydrastine with formation of *l*-β-hydrastine, is described below.

Experimental.

l-β-*Narcotine*.—A solution of narcotine (*l*-α-narcotine) (70 g.) and potassium hydroxide (70 g.) in methyl alcohol (1000 c.c.) was refluxed for 3½ days and then diluted with water and acidified by hydrochloric acid. The methyl alcohol was evaporated on the steam-bath, and the bases precipitated from the cooled solution by ammonia. The crude material (m. p. 135—145°) was extracted with boiling ethyl alcohol (600 c.c.), and the crystals remaining undissolved were isolated (35 g.). This product is substantially *l*-β-narcotine, as the following examination shows. The base (30 g.) was dissolved in ethyl acetate (350 c.c.), allowed to cool to room temperature, and the crystals collected after 2 hours (21 g., m. p. 175°; m. p. 176° after recrystallisation from alcohol; mixed with *l*-α-narcotine, m. p. 145—150°). A further crop, m. p. 172—173°, separated on keeping the solution in the ice-chest. The mother-liquor from this was used to dissolve a second quantity (17·5 g.) of the original base, sparingly soluble in alcohol, and the crystals obtained on cooling (16·8 g.) consisted of almost pure *l*-β-narcotine, m. p. 173—174°. The separation of the bases in the mother-liquor from the original alcohol extraction proved very tedious. Unsuccessful separations were attempted by fractionation from alcohol and ethyl acetate, and by the crystallisation of the hydrochlorides, nitrates, and sulphates. *l*-α-Narcotine picrate is the more sparingly soluble in hot alcohol, and a long series of fractionations of this derivative brought about the desired separation; the process was not, however, sufficiently clean-cut to enable us to advance an estimate of the relative proportion of *l*-α-narcotine and *l*-β-narcotine produced. We found no evidence of the formation of α- or β-gnoscopine. Experiments are in progress having for their object the study of this and related equilibria by polarimetric methods, but the formation of colouring matters and other by-products is proving a difficulty.

l-β-*Narcotine* crystallises from alcohol in glistening leaflets or plates, or from acetone in more compact prisms, m. p. 176° (Found: C, 63·8; H, 5·5; N, 3·2. $C_{22}H_{23}O_7N$ requires C, 63·9; H, 5·5; N, 3·4%). {0·3 G. in 25 c.c. of chloroform at 18° (*l* = 20 cm.) gave α — 2·42°; whence $[\alpha]_{546}$ — 101°. 0·3 G. (1 mol.) in 1·45 c.c. *N*-hydrochloric acid (2 mols.) made up to 25 c.c. gave α — 1·42°, $[\alpha]^{18°}_{546}$ — 59·2°. 0·3 G. (1 mol.) in 7·26 c.c. *N*-hydrochloric acid (10 mols.) made up to 25 c.c. gave α — 1·44°, $[\alpha]^{18°}_{546}$ — 60·0°. Under precisely the same conditions *l*-α-narcotine gave $[\alpha]^{18°}_{546}$ — 246°, + 50·4°, and + 54·6° respectively.}

The *hydrochloride* crystallised from dilute aqueous hydrochloric acid in colourless needles, readily soluble in water but more sparingly soluble than *l*-α-narcotine hydrochloride (Found, in air-dried specimens: C, 55·0; H, 5·7; N, 3·0; Cl, 8·2, 7·4, 7·5. $C_{22}H_{23}O_7N,HCl,1·5H_2O$ requires C, 55·5; H, 5·7; N, 2·9; Cl, 7·4%). The *hydrogen sulphate* crystallises in white needles (Found: C, 51·0; H, 5·3; N, 2·7; S, 5·5. $C_{22}H_{23}O_7N,H_2SO_4$ requires C, 51·7; H, 4·9; N, 2·7; S, 6·2%, indicating the presence of some normal sulphate). The *picrate* crystallised from alcohol below 40° in thin yellow rods, m. p. 118° after drying at 100° (Found: C, 51·7; H, 4·2; N, 8·7. $C_{22}H_{23}O_7N,C_6H_3O_7N_3$ requires C, 52·3; H, 4·1; N, 8·7%).

The *methiodide* was prepared by refluxing a solution of the base in absolute alcohol with an excess of methyl iodide for 8 hours, and concentrating and cooling the solution; it recrystallised from hot water in white prisms, m. p. 208° (Found: C, 49·7; H, 4·7; N, 2·2; I, 22·5. $C_{22}H_{23}O_7N,CH_3I$ requires C, 49·8; H, 4·7; N, 2·5; I, 22·9%). The addition of alcoholic iodine to a solution of this salt in alcohol precipitated *l*-β-*narcotine methotri-iodide*, which is insoluble in hot or cold water and crystallises from alcohol in long, reddish-brown rods, m. p. 187·3° (Found: C, 34·2; H, 3·4; N, 2·0. $C_{22}H_{23}O_7N,CH_3I_3$ requires C, 34·1; H, 3·2; N, 1·7%). This salt is obtained when a solution of *l*-β-narcotine methiodide is treated with 1 equiv of sodium hydroxide; on the addition of an excess of alkali and on boiling, narceine is formed and may be precipitated by passage of carbon dioxide. Frankforter and Keller (*J. Amer. Chem. Soc.*, 1900, **22**, 61) obtained an analogous salt from natural narcotine when they submitted the methiodide of the base to the action of chlorine in alcoholic solution.

The conversion of *l*-β-narcotine into narceine is best accomplished as follows. The methosulphate, prepared from pure dry materials in hot benzene solution, is a viscid oil; it is washed with light petroleum, then dissolved in water, the solution rendered alkaline by means of potassium hydroxide, boiled for 10 minutes, and just acidified with acetic acid. The characteristic, thread-like crystals obtained on standing were recrystallised, m. p. 178—179°, alone or mixed with authentic narceine of natural origin.

Oxidation of *l*-β-narcotine by means of nitric acid under the conditions used for the preparation of cotarnine from *l*-α-narcotine did not succeed, and the mixture was heated to 75° (*l*-α-narcotine oxidises easily at 45—50°) and kept at that temperature until the addition of ammonia produced no precipitate. Cotarnine was then isolated in the known manner, and recognised by conversion into anhydrocotarninenitromethane, colourless prisms, m. p. 129° alone or mixed with an analysed specimen (Hope and Robinson, J., 1911, **99**, 2114). The formation of opianic acid was also detected through the conversion of this product of the reaction, isolated by means of ether extraction of the acidified solution after removal of cotarnine, into hemipinimide in the usual way. The hemipinimide had m. p. 229° alone or mixed with an authentic specimen.

l-α-Narcotine could not be racemised or partly racemised by long refluxing with 10% methyl-alcoholic hydrogen chloride, being recovered unchanged (cf. Rabe, *Annalen*, 1910, **377**, 233, for the similar experience with aqueous sulphuric acid); but whereas Rabe (*loc. cit.*) reports that *l*-α-narcotine yields α-gnoscopine when heated for 8 hours with aqueous acetic acid at 120°, we find that *l*-β-narcotine is recovered unchanged after this treatment.

d-β-*Narcotine*.—This base was obtained from *d*-α-narcotine (Perkin and Robinson, *loc. cit.*) under conditions closely resembling those described above for the partial racemisation of *l*-α-narcotine. The results were the same, and the base was the true diastereoisomeride of *l*-β-narcotine; plates from alcohol, m. p. 176° (Found: C, 63·7; H, 5·5%), $[\alpha]_{5461}^{18°}$ + 103° (in chloroform). When hot solutions of 50 mg. each of *d*-β- and *l*-β-narcotine in alcohol were mixed and cooled, 96 mg. of pure β-gnoscopine, m. p. 180°, separated. The base had the crystalline habit of β-gnoscopine, and the m. p. was not lowered on admixture with a specimen prepared from nitro-β-gnoscopine (Hope and Robinson, *loc. cit.*).

Conversion of l-β- *into* l-α-*Narcotine*.—This experiment was carried out under the conditions described for the reverse change, and the *l*-α-narcotine was isolated in the form of the picrate, m. p. 177°. It was recovered from the purified derivative, and recognised by means of m. p. and mixed m. p.

Interconversion of α- *and* β-*Gnoscopine*.—The usual conditions (refluxing with methyl-alcoholic potash for 3½ days) were employed, and the separation of the bases effected by taking advantage of the more sparing solubility of α-gnoscopine in alcohol and of β-gnoscopine nitrate in water. α-Gnoscopine was recovered, and the β-gnoscopine obtained crystallised from alcohol in colourless prismatic needles, m. p. 180° alone or mixed with an authentic specimen (Found: C, 63·9; H, 5·7%). The picrate was also prepared, m. p. 198° alone or mixed with an authentic specimen. In the same way β-gnoscopine was converted into α-gnoscopine, m. p. 230° alone or mixed with an authentic specimen (from opium), and thus the existence of an equilibrium was established; the quantitative aspect is under examination.

It is known that β-gnoscopine affords α-gnoscopine almost completely when it is heated with aqueous alcohol at 100° in a pressure bottle (Hope and Robinson, *loc. cit.*), but the reverse change has not previously been studied. α-Gnoscopine (5 g.), alcohol (100 c.c.), and water (25 c.c.) were heated in a closed bottle at 100° for 120 hours. On separation, 4·32 g. of α-gnoscopine were recovered, but 0·07 g. of β-gnoscopine was also isolated (identification as usual; yield, 1·4%).

Conversion of l-β-*Narcotine into Gnoscopines*.—A mixture of *l*-β-narcotine (2 g.) and alcohol (60 c.c.) was heated in a closed vessel at 175° for 6 hours. Much decomposition occurred, and on concentrating the dark solution, meconin (0·32 g.) separated, m. p. 98° alone or mixed with authentic material. A small quantity of α-gnoscopine, m. p. 229—230°, was obtained from the mother-liquor. After refluxing a mixture of *l*-β-narcotine (2 g.), alcohol (32 c.c.), and water (32 c.c.) for 8 days, α-gnoscopine (0·214 g.) and β-gnoscopine (0·022 g.) could be separated in a pure condition.

l-α-*Hydrastine*.—A mixture of hydrastine (natural alkaloid) (10 g.), potassium hydroxide (10 g.), and methyl alcohol (150 c.c.) was refluxed for 5 days, then diluted with water, acidified with hydrochloric acid, and concentrated on the steam-bath until most of the methyl alcohol had been removed. On cooling, pearly crystals of a hydrochloride separated, and this salt was collected, washed with dilute hydrochloric acid, dissolved in hot water, and the base precipitated with ammonia, collected, and crystallised from alcohol (150 c.c.). The colourless prisms (5·3 g.),

m. p. 159—160°, consisted of nearly pure l-α-*hydrastine*, and after several recrystallisations from ethyl acetate and from alcohol the m. p. was only raised to 162° (Found : C, 65·7; H, 5·4; N, 3·7. $C_{21}H_{21}O_6N$ requires C, 65·8; H, 5·5; N, 3·7%). {0·3 G. in 25 c.c. of chloroform at 18° (l = 20 cm.) gave α — 3·90°; whence $[\alpha]_{546}^{18°}$ — 163°. Under the same conditions natural hydrastine (*l*-β-hydrastine) gave $[\alpha]_{546}^{18°}$ — 68·3°.}

The mother-liquor from the sparingly soluble hydrochloride was basified, and afforded unchanged *l*-β-hydrastine (2·1 g.) and a further quantity (0·6 g.) of *l*-α-hydrastine. The separation was laborious, and the methods employed were crystallisation of the bases from methyl alcohol for the isolation of *l*-β-hydrastine, and formation of the sparingly soluble hydrochloride of *l*-α-hydrastine from the mother-liquors.

The *hydrochloride* crystallised from dilute hydrochloric acid, in which it is much more sparingly soluble than *l*-β-hydrastine hydrochloride, in well-shaped, white, oblong plates, pointed at one end, or in more slender needles, m. p. *ca.* 237° (Found : C, 60·4; H, 5·4; N, 3·4. $C_{21}H_{21}O_6N$,HCl requires C, 60·0; H, 5·3; N, 3·3%). The *picrate* crystallised from 95% alcohol at 30° in deep yellow, squat prisms, m. p. 172° after drying at 100° (Found : C, 52·8; H, 3·9; N, 9·1. $C_{21}H_{21}O_6N$,$C_6H_3O_7N_3$ requires C, 52·9; H, 4·0; N, 9·2%).

A specimen of the *methiodide*, m. p. 206°, prepared from the components in alcoholic solution appeared to be homogeneous but was ultimately found to be a mixture containing the hydriodide. The pure derivative was prepared by dissolving *l*-α-hydrastine in an excess of methyl iodide, raising the liquid to the b. p. several times, and then keeping it for 12 hours in a closed vessel. The white crystals were collected, and crystallised from hot water and then from alcohol in prisms, m. p. 222° (Found : C, 50·7; H, 4·7; I, 24·5. $C_{21}H_{21}O_6N$,CH_3I requires C, 50·3; H, 4·6; I, 24·2%).

This methiodide (1·07 g.) was dissolved in hot water (50 c.c.), and potassium hydroxide added until the solution was strongly alkaline; an immediate white precipitate quickly changed to a golden oil, which partly dissolved as the solution was boiled for 10 minutes. This substance was collected and washed; it crystallised from 50% or 95% alcohol in soft, pale yellow needles, m. p. *ca.* 50° (but not to a clear liquid; at about 75° gas was evolved but again the liquid was not transparent). The substance could not be obtained pure; its solutions exhibited a green fluorescence, and in this and other properties it closely resembles methylhydrastine, of which it is probably a stereoisomeride. The aqueous solution decanted from the oil was just acidified with acetic acid, and thereupon methylhydrasteine separated. The substance crystallised twice from hot water in soft, slender, white needles, m. p. 150°.

The equilibrium in boiling methyl-alcoholic potassium hydroxide greatly favours the production of *l*-α-hydrastine, but some *l*-β-hydrastine is formed from the pure α-base. *l*-α-Hydrastine (2 g.) was refluxed for 3 days with methyl alcohol (30 c.c.) and potassium hydroxide (2·0 g.). By the same procedure as before, *l*-α-hydrastine (1·02 g.) was recovered at once, and the residual mixture could be roughly resolved by mechanical separation of the crystals. In this way, *l*-β-hydrastine (15 mg.) was obtained in a pure condition, m. p. 132° alone or mixed with natural hydrastine.

Notes on the Synthesis of Hydrastines-a *and* -b.—We are much indebted to Professor J. S. Chamberlain of Amherst, Mass., U.S.A., for the following. Encountering difficulty in the reduction of nitro-*r*-hydrastine as described by Hope, Pyman, Remfry, and Robinson (*loc. cit.*), it was decided to collect the double tin salt of aminohydrastine and work this up separately. This led to the isolation of practically pure aminohydrastine-*a*.

Nitrohydrastine (20 g.) was dissolved as far as possible in cold 80% acetic acid (100 c.c.), and granulated tin (10 g.) added. The mixture was cooled to 10°, and a solution of crystallised stannous chloride (50 g.) in concentrated hydrochloric acid (80 c.c.) was added with cooling in running water to below 10°. The salt began to separate after 20 minutes, and after 6 hours it was collected, washed, and stirred with water (1000 c.c.). The base was precipitated by the addition of 50% potassium hydroxide (150 c.c.), and was washed and dried (13·7 g., m. p. 208—215°, yield, 74%). It is to be noted that in this process vigorous treatment with alkali is avoided, and transformations such as those described in this memoir could not occur under such conditions.

In the diazotisation of aminohydrastine-*a*, according to Hope *et al.* (*loc. cit.*), it is essential to pulverise very finely the aminohydrastine hydrochloride and to stir the solution vigorously by mechanical means during the *very* slow addition of the nitrite (this should last 2½ hours). The amino-salt gradually passes into solution, but it is replaced by the yellow diazo-salt, and after all the nitrite has been introduced stirring should be continued for at least 1 hour (yield, 69% of material, m. p. 173°).

The yield of hydrastine-*a* obtained by the oxidation of hydrazinohydrastine-*a* was 32%.

Complete Racemisation of l-β-*Hydrastine. Formation of Ethyl*chano*hydrastine.*—A large number of experiments have been made with the object of procuring specimens of the inactive isomerides of hydrastine, but with indifferent success. In two experiments, *l*-β-hydrastine (5 g.) was heated at 95° under pressure with 50% ethyl alcohol (160 c.c.) and 77% and 73% of the base was recovered. In the second case, 6% of constant-crystallising mixture was the residue, but in the first example a new *substance* crystallising from alcohol in glistening, pale brownish-yellow, prismatic needles, m. p. 134°, was obtained (0·3% yield) (Found: C, 67·2; H, 6·3; N, 3·5. $C_{22}H_{25}O_6N$ requires C, 67·2; H, 6·1; N, 3·4%). A mixture with hydrastine showed a large depression of m. p. The substance is a base and an ethyl ester, since it furnished ethyl alcohol on boiling with aqueous sodium hydroxide (10%). Owing to the very small quantity available, the substance could not be more fully investigated but it appears certain that it is the ethyl ester of the unsaturated acid corresponding to hydrastine. If we add that we regard it as a stilbene derivative, these words completely describe our view of its constitution.

On another occasion, *l*-β-hydrastine (4·15 g.) was heated at 100—110° for 24 hours with aqueous alcohol, and we were then able to isolate, in addition to the usual proportion of the unchanged base, hydrastine-*a* (4·7%), hydrastine-*b* (1·25%), an unidentified substance, m. p. 150—155° (0·6%), and constant-crystallising residue (17·7%). A repetition (8 g. of the alkaloid) gave unchanged *l*-β-hydrastine, hydrastine-*a* (2·9%), ethyl*chano*hydrastine (0·7%), and 7·1% of residual crystalline material. A third experiment under similar conditions (8 g. of base), but at 110—120°, gave 5·27 g. of crystallisable material. This was directly treated with methyl-alcoholic potassium hydroxide as described above (*l*-β-hydrastine ⟶ *l*-α-hydrastine) and there were then isolated *l*-α-hydrastine (27·3%), hydrastine-*b* (3·8%), *l*-β-hydrastine (4·2%), and 3·4% of residual mixed hydrastines.

Again, the alkaloid (20 g.) was heated with 50% alcohol at 100° for 24 hours and then treated with methyl-alcoholic potash. The products isolated were *l*-α-hydrastine (45·6%), *l*-β-hydrastine (8·9%), hydrastine-*a* (0·9%), and 6·4% of residual crystalline bases.

The hydrastine-*a* obtained in this way was in every respect identical with the synthetic product. It had m. p. 135°, alone or mixed with a specimen obtained from hydrazinohydrastine-*a* by the method of Hope *et al.* (*loc. cit.*). For further confirmation, the picrates were prepared and crystallised from methyl ethyl ketone in identical fashion, m. p. 218—220° (decomp.) alone or mixed.

Other Transformations of the Hydrastines.—Hydrastine-*a* (0·550 g.) was refluxed for 36 hours with methyl alcohol (10 c.c.) and potassium hydroxide (0·55 g.). The recovered bases were fractionated from alcohol, and hydrastine-*b* (0·166 g.) was isolated (Found: C, 65·5; H, 5·5; N, 3·9. Calc. for $C_{21}H_{21}O_6N$: C, 65·8; H, 5·5; N, 3·7%). The base had m. p. 150°, alone or mixed with hydrastine-*b* prepared from hydrazinohydrastine-*b*. An adequate supply of hydrastine-*b* was not available for the investigation of its transformation into hydrastine-*a*.

A small quantity of impure hydrastine-*b* was obtained by prolonged heating of *l*-α-hydrastine with acetic acid; *l*-β-hydrastine was not racemised by this reagent. Similarly, *l*-α-hydrastine (5 g.), heated with alcohol (100 c.c.) and water (25 c.c.) at 100° for 96 hours, was largely unchanged (4·35 g.), but a few mg. of hydrastine-*b*, m. p. 149°, were isolated.

Table of m. p.'s and mixed m. p.'s.

(It is assumed that hydrastine-*b* is *dl*-α-hydrastine.)

	Narcotine.	Hydrastine.		Narcotine.	Hydrastine.
l-α	176°	161°	*l*-α + *l*-β	145°	116°
l-β	176	132	*dl*-α + *dl*-β	170	121
dl-α	230	150	*l*-α + *dl*-α	173	145
dl-β	180	135	*l*-β + *dl*-α	168	119
			l-α + *dl*-β	156	143
			l-β + *dl*-β	170	122

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