360. *A New Route to the Phthalide-*isoquinoline *Bases, and a Synthesis of (−)-Hydrastine.*

By Robert D. Haworth and A. Reginald Pinder.

A new method for the synthesis of alkaloids of the hydrastine type has been developed. The racemic bases, hydrastine-*a* and -*b*, obtained previously by another method by Hope, Pyman, Remfry, and Robinson (*J.*, 1931, 236) have been prepared, and hydrastine-*a* has been resolved into (+)- and (−)-forms, the latter of which was identical with (−)-hydrastine from natural sources.

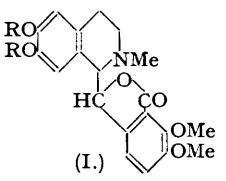
Similar reactions led to the synthesis of two racemic modifications of cordrastine, but attempts to resolve the bases into their optically active forms have been unsuccessful.

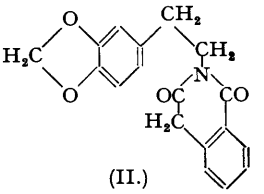
The synthetic approach to the lactonic 1-benzyl*iso*quinoline alkaloids of type (I) is confined to the method of Perkin and Robinson (*J.*, 1911, **99**, 775) (see also Hope and Robinson, *J.*, 1911, **99**, 1153) in which an *iso*quinoline ψ-base is condensed with a phthalide or its nitro- or iodo-derivative. In this way (±)-narcotine and (±)-*iso*narcotine (α- and β-gnoscopine) were prepared and the former was resolved into its optically active forms (Perkin and Robinson, *loc. cit.*, p. 788); later two inactive modifications of hydrastine (I; RR = CH_2) known as hydrastine-*a* and -*b* were synthesised (Hope, Pyman, Remfry, and Robinson, *J.*, 1931, 236) but resolution was not effected.

The isolation of several new alkaloids of type (I), including bicuculline from *Dicentra cucullaria*, etc. (Manske, *Canadian J. Res.*, 1938, **8**, 142), adlumine from *Adlumia fungosa*

(Manske, *ibid.*, p. 404), cordrastine (I; R = Me) from *Corydalis aurea* (Manske, *ibid.*, 1938, **16**, *B*, 81) and others (Manske, *ibid.*, 1933, **8**, 210, 404; 1936, **14**, *B*, 325, 347, 354) has revived interest in this field, and the ψ-base-phthalide reactions have been employed to synthesise (±)-bicuculline (Groenewoud and Robinson, *J.*, 1936, 199).

The present communication describes an alternative series of reactions which have been developed for the synthesis of alkaloids of type (I). During some preliminary experiments a detailed examination of the properties of *N*-(2-3′ : 4′-methylenedioxyphenylethyl)homophthalimide (II) showed that the amic acid, m. p. 158—159°, described by the previous workers


(I.)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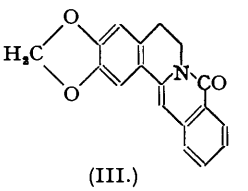
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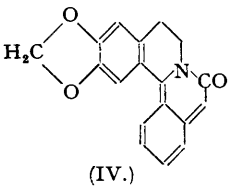
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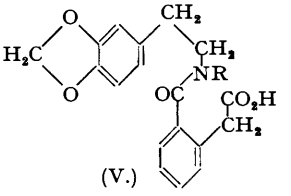
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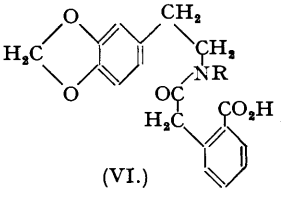
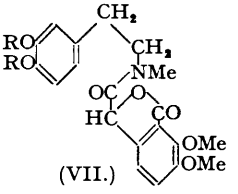

(VI.)

(Haworth, Perkin, and Pink, *J.*, 1925, **127**, 1718) was impure, and that, in fact, alkaline hydrolysis of the imide (II) yielded a mixture of two isomeric *amic acids*, m. p. 163° and 154° respectively. The higher-melting acid gave a *methyl* ester, m. p. 96°, and the lower-melting acid a *methyl* ester, which existed in a labile form, m. p. 93·5°, and a stable form, m. p. 128°. When 2-3′ : 4′-methylenedioxyphenylethylamine was condensed with homophthalic anhydride in benzene solution, the amic acid, m. p. 154°, was obtained in high yield, and the isomeric acid was not isolated. Heating either of the amic acids yielded the imide (II), but the methyl esters showed a different behaviour when treated with phosphorus oxychloride in toluene solution; the ester, m. p. 128°, gave 2 : 3-methylenedioxyoxyprotoberberine (III), m. p. 180°, and the ester, m. p. 96°, gave the orange-red 2 : 3-methylenedioxyoxy*iso*protoberberine (IV), m. p. 225° (cf. Haworth, Perkin and Pink, *loc. cit.*). It is therefore probable that the amic acids, m. p. 163° and 154°, have the structures (V) and (VI) (R = H) respectively, and these conclusions are supported by measurements of the dissociation constants of the two acids. Wegscheider's observations (*Monatsh.*, 1903, **24**, 930) on the relative strengths of the carboxyl groups in homophthalic acid suggest that the acid (VI) should be stronger than (V), and we find that the acid, m. p. 154°, with $K = 1{\cdot}9 \times 10^{-5}$ is stronger than the acid, m. p. 163°, which has $K = 6{\cdot}3 \times 10^{-6}$.

Condensation of homophthalic anhydride and *N*-methyl-2-3′ : 4′-methylenedioxyphenylethylamine gave an amic acid, m. p. 151·5°, probably N-*methyl*-N-2-3′ : 4′-*methylenedioxyphenylethyl*-o-*carboxyphenylacetamide* (VI; R = Me), but attempts to cyclise this acid or the corresponding *methyl* ester, m. p. 88°, with phosphorus oxychloride or pentachloride, or phosphoric oxide, failed to yield any basic material and the reactions were abandoned.

A modification of the method used by Perkin, Rây, and Robinson (*J.*, 1925, **127**, 741) for the synthesis of oxyberberine has been developed into a general method for the synthesis of bases of type (I). Meconine-α-carboxyl chloride (Perkin, Rây, and Robinson, *loc. cit.*) and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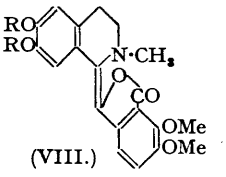
(VIII.)

N-methyl-2-3′ : 4′-methylenedioxyphenylethylamine reacted readily in benzene to give N-*methyl*-N-(2-3′ : 4′-*methylenedioxyphenylethyl*)*meconine*-α-*carboxyamide* (VII; RR = CH_2), m. p. 137°,

which was converted in 50—55% yield into *dehydrohydrastine* (VIII; RR = CH_2), m. p. 205°, by the action of phosphorus oxychloride. This orange-red compound (VIII) was soluble in warm dilute hydrochloric acid, but when the solution was boiled decomposition gradually occurred and oxyhydrastinine and meconine were produced. Dehydrohydrastine was rapidly reduced in acetic acid solution in the presence of a platinic oxide catalyst to a mixture of two isomeric forms of hydrastine (I; RR = CH_2) which were separated by taking advantage of the differing solubilites of their respective *picrates* in acetone. The acetone-insoluble salt yielded hydrastine-*a*, m. p. 139°, and the soluble salt gave hydrastine-*b*, m. p. 152°, and the bases gave no depression of the melting points when mixed with samples kindly supplied by Sir Robert Robinson.

Marshall, Pyman, and Robinson (*J.*, 1934, 1315) failed to resolve the racemic hydrastine bases, but as a result of a comparative study of the epimerisation of narcotine and hydrastine they concluded that naturally occurring (−)-hydrastine was probably an optically active form of hydrastine-*a*. The new synthesis has made it possible to prepare relatively large amounts of hydrastine-*a* and -*b* and to subject the diastereoisomeric bases to a series of careful resolution experiments. Although we have converted hydrastine-*b* into the hydrogen (+)-tartrate, (+)- and (−)-*camphor*-10-*sulphonate*, and (+)-*bromocamphor*-10-*sulphonate*, it has not been possible to resolve these crystalline derivatives, and (±)-hydrastine-*b* was recovered from all fractions. Similarly the *hydrogen* (+)-*tartrate* of hydrastine-*a* resisted resolution but the (+)-*camphor*-10-*sulphonate* was separated by crystallisation from water into needles, m. p. 120—122°, which had $[\alpha]_D^{15} = -25{\cdot}5°$ unchanged by further crystallisation, and a semi-solid fraction which was obtained from the mother-liquors. The needles were apparently an inseparable mixture of the (+)-camphor-10-sulphonates of the (±)- and the (+)-hydrastine-*a* base; decomposition of the salt yielded a crude base with $[\alpha]_D^{16} = +26{\cdot}7°$ which was separated by crystallisation from methyl alcohol into (±)-hydrastine-*a*, m. p. 138—139°, $[\alpha]_D^{15} = 0°$, and (+)-*hydrastine*-a, m. p. 131—132° $[\alpha]_D^{19} = +42{\cdot}2°$. The semi-solid fraction from the mother-liquors from the (+)-camphor-10-sulphonate gave a crude base with $[\alpha]_D^{15} = -30{\cdot}2°$, which yielded (−)-*hydrastine*-a, m. p. 131—132°, $[\alpha]_D^{14} = -42{\cdot}1°$, on crystallisation from methyl alcohol. This base was identical with a specimen of (−)-hydrastine, kindly supplied by Messrs. T. & H. Smith of Edinburgh, which had $[\alpha]_D^{14} = -41{\cdot}7°$ and did not depress the melting point of the synthetic (−)-base.

Structure (I; R = Me) has been suggested for cordrastine, and two racemic modifications for this base have been synthesised by methods similar to those used in the synthesis of hydrastine-*a* and -*b*. *N*-Methyl-2-3′ : 4′-dimethoxyphenylethylamine reacted with meconine-α-carboxyl chloride, giving the *amide* (VII; R = Me), which was converted by the action of phosphorus oxychloride into *dehydrocordrastine* (VIII; R = Me). This yellow base was reduced catalytically to a mixture of two racemic modifications, cordrastine I, m. p. 155—156°, and cordrastine II, m. p. 118—119°. Cordrastine I, which was sparingly soluble in methyl or ethyl alcohol, gave crystalline (+)- and (−)-*camphor*-10-*sulphonates* and a crystalline (+)-*bromocamphorsulphonate*, but attempts to resolve these were unsuccessful. Of the salts with optically active acids, only the *hydrogen* (−)-*tartrate* of cordrastine II, m. p. 118—119°, was crystalline, and attempts to resolve this salt were unsuccessful.

Experimental.

Hydrolysis of N-(2-3′ : 4′-*Methylenedioxyphenylethyl*)*homophthalimide* (II).—This imide (4 g.) was prepared and hydrolysed as described by Haworth, Perkin, and Pink (*loc. cit.*). The crude amic acid was separated by fractional crystallisation from methyl alcohol into o-*carboxymethyl*-N-(2-3′ : 4′-*methylenedioxyphenylethyl*)*benzamide* (V; R = H) (1·8 g.), m. p. 163—164° (Found: equiv., 326·5; C, 66·4; H, 5·0%. $C_{18}H_{17}O_5N$ requires equiv., 327; C, 66·1; H, 5·2%), and N-(2-3′ : 4′-*methylenedioxyphenylethyl*)-o-*carboxyphenylacetamide* (VI; R = H) (1·7 g.), glistening needles, m. p. 153° (Found: C, 65·4; H, 5·4%; equiv., 326·8. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2%; equiv., 327).

Esterification of the silver salts with methyl iodide in ethereal suspension yielded the methyl esters. The *methyl* ester of (V; R = H) crystallised from ether in glistening colourless needles, m. p. 95—96° (Found: C, 66·7; H, 5·7. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·6%). The *methyl* ester of (VI; R = H) separated from methyl alcohol as prismatic needles, m. p. 93·5° (Found: C, 66·7; H, 5·7. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·8%), or long feathery needles, m. p. 128° (Found: C, 66·7; H, 5·8%); inoculation of a methyl-alcoholic solution of the lower-melting modification with the form of m. p. 128° resulted in the conversion of the former into the latter, but the reverse change was not realised.

Condensation of 2-3′ : 4′-*Methylenedioxyphenylethylamine and Homophthalic Anhydride.*—A mixture of the amine (0·5 g.) and the anhydride (0·5 g.) was refluxed in dry benzene (8 c.c.) for 2 hours during which a crystalline solid gradually separated. The cooled mixture was shaken with 5% sodium hydroxide solution (20 c.c.), and the alkaline extract was acidified; the crude acid, which slowly solidified, crystallised from methyl alcohol in glistening prismatic needles (0·9 g.), m. p. 152—153°, identical with the amic acid (VI; R = H) described above.

Cyclisation of the Methyl Esters, M. p. 128° *and* 95—96°.—The ester, m. p. 128° (0·5 g.), dry toluene (3·5 c.c.) and phosphorus oxychloride (1·25 c.c.) were gently refluxed for 45 minutes. The toluene and oxychloride were removed under reduced pressure and the residue was taken up with chloroform. The product crystallised from methyl alcohol in colourless needles, m. p. 180°, which gave no depression in m. p. with 2 : 3-methylenedioxyoxyprotoberberine (III).

The ester, m. p. 95°, underwent cyclisation more slowly; after 2 hours' refluxing the product, isolated as described above, crystallised from dilute acetic acid in orange-red needles, m. p. 225°, which gave no depression in m. p. with 2 : 3-methylenedioxyoxy*iso*protoberberine (IV).

N-*Methyl*-N-(2-3′ : 4′-*methylenedioxyphenylethyl*)-o-*carboxyphenylacetamide* (VI; R = Me).—A benzene solution (20 c.c.) of *N*-methyl-2-3′ : 4′-methylenedioxyphenylethylamine (2·0 g.) and homophthalic anhydride (1·8 g.) was refluxed for 1½ hours. The cooled mixture was extracted with 5% sodium hydroxide solution (50 c.c.), and the *amic acid* (VI; R = Me) was recovered and crystallised from methyl alcohol; glistening white plates (3·7 g.), m. p. 151·5° (Found: C, 66·6; H, 5·6. $C_{19}H_{19}O_5N$ requires C, 66·8; H, 5·6%), were obtained. The *methyl* ester, prepared from the silver salt, crystallised from ether in colourless prisms, m. p. 88° (Found: C, 67·6; H, 5·8. $C_{20}H_{21}O_5N$ requires C, 67·6; H, 5·9%).

N-*Methyl*-N-(2-3′ : 4′-*methylenedioxyphenylethyl*)*meconine-α-carboxyamide* (VII; RR = CH_2).—Meconine-α-carboxyl chloride (prepared from 10 g. of the corresponding acid as described by Perkin, Rây, and Robinson, *loc. cit.*) in benzene (25 c.c.) was added drop-wise and with cooling to a mixture of *N*-methyl-*N*-2-3′ : 4′-methylenedioxyphenylethylamine (8·0 g.) in benzene (20 c.c.) and N-sodium hydroxide solution (50 c.c.). The mixture was shaken for 3 hours, and after 12 hours the *amide* (VII; R = CH_2) which gradually separated was collected, washed with water, and crystallised from methyl alcohol. Elongated colourless prisms (12 g.), m. p. 136—137° (Found: C, 63·0; H, 5·5. $C_{21}H_{21}O_7N$ requires C, 63·2; H, 5·3%), were obtained.

Dehydrohydrastine (VIII; RR = CH_2).—The amide (VII; RR = CH_2) (1·0 g.) and phosphorus oxychloride (6·0 c.c.) were gently refluxed for 50 minutes. The oxychloride was removed under reduced pressure from the dark red solution, and the residual red gum was washed with light petroleum (b. p. 40—60°), taken up in methyl alcohol (3 c.c.), cooled to 0°, and basified by the gradual addition of methyl-alcoholic ammonia (5 c.c. of saturated solution). The mixture was poured into water (30 c.c.), extracted twice with methylene dichloride, dried (Na_2SO_4), and freed from solvent. The residual oil solidified on trituration with a little methyl alcohol, and the product crystallised from ethyl acetate in glistening orange-red elongated prisms (or needles) (0·5 g.), m. p. 204—205° (Found: C, 66·1; H, 5·0. $C_{21}H_{19}O_6N$ requires C, 66·2; H, 5·0%). This interesting highly-coloured *base* was decomposed by boiling it with dilute hydrochloric acid to give oxyhydrastinine, m. p. 98°, and meconine, m. p. 102°; this degradation confirmed its structure. It was sparingly soluble in cold dilute acids, methyl or ethyl alcohol, or benzene, but soluble in chloroform, yielding an orange-red solution. It did not appear to be reduced by zinc in dilute hydrochloric acid.

Hydrastine-a *and Hydrastine*-b.—Finely powdered dehydrohydrastine (VIII; RR = CH_2) (0·75 g.) was suspended in glacial acetic acid (60 c.c.) and shaken with platinic oxide (10 mg.) in an atmosphere of hydrogen for 2 hours. The colourless solution was filtered, the solvent removed under reduced pressure, and the residual gum basified with aqueous ammonia and extracted with methylene dichloride. After drying of the extract the solvent was removed, and the product was taken up in methyl alcohol (4 c.c.) and mixed with a solution of picric acid (0·42 g.) in methyl alcohol (3 c.c.). The mixture was warmed for a few minutes, and next morning the crude picrate (1·15 g.) was collected and refluxed with acetone (15 c.c.) for ½ hour. The residue (0·5 g.) separated from a large volume of methyl ethyl ketone in glistening yellow prisms, m. p. 217—218° (Found: C, 52·9; H, 4·1. Calc. for $C_{27}H_{24}O_{13}N_4$: C, 52·9; H, 3·9%), which gave no depression in m. p. when mixed with hydrastine-*a* picrate.

The acetone filtrate, on concentration to about 5 c.c. gave the *hydrastine*-b *picrate*, which separated from acetone in clusters of stout yellow prisms, m. p. 197—198° (Found: C, 52·9; H, 4·2%).

The picrates (0·25 g.) were decomposed with methyl-alcoholic ammonia; most of the methyl alcohol was then removed and the residue, after the addition of dilute aqueous ammonia, was extracted first with methylene dichloride (5 c.c.) and then with ether (10 c.c.). The combined extracts were washed several times with dilute ammonia solution and dried, the solvents removed, and the bases recovered quantitatively. Hydrastine-*a* crystallised from ether or methyl alcohol in glistening stout prisms, m. p. 138—139° (Found: C, 65·7; H, 5·5. Calc. for $C_{21}H_{21}O_6N$: C, 65·8; H, 5·5%).

Hydrastine-*b* separated from methyl alcohol in stout colourless prisms, m. p. 151—152° (Found: C, 65·5; H, 5·4%). The two bases showed no depression in m. p. when mixed with specimens of hydrastine-*a* or -*b* respectively.

Attempts to resolve Hydrastine-b.—*Hydrastine*-b *hydrogen* (+)-*tartrate* was prepared by warming equimolecular quantities of base and (+)-tartaric acid in water, extra tartaric acid being added in small quantities until dissolution was complete and until the unchanged base did not separate on cooling; it separated from water in clusters of felted needles, m. p. 60—70° (Hope, Pyman, Remfry, and Robinson, *J.*, 1931, 236, give m. p. 65—70°) (Found: C, 49·9; H, 5·6; H_2O, 13·1. Calc. for $C_{25}H_{27}O_{12}N,4H_2O$: C, 49·6; H, 5·8; H_2O, 13·3%), which after being dried *in vacuo* over phosphoric oxide melted at 115—120° and had $[\alpha]_D^{23}$ = +8·3° in water (*c*, 1·28). The (+)-*camphor*-10-*sulphonate*, prepared in alcoholic solution, separated in small colourless prisms, m. p. 183—186° (Found: C, 60·5; H, 6·0. $C_{31}H_{37}O_{10}NS$ requires C, 60·5; H, 6·0%), $[\alpha]_D^{17}$ = +7·5° in water (*c*, 0·86). The (−)-*camphor*-10-*sulphonate* separated from alcohol in slender, colourless prisms, m. p. 180—185° (Found: C, 60·1; H, 6·0%), $[\alpha]_D^{22}$ = −13·0° in water (*c*, 0·5). The (+)-*bromocamphor*-10-*sulphonate*, prepared in aqueous solution, separated from methyl alcohol in clusters of colourless elongated prisms, m. p. 225—230°, with slight previous softening (Found: C, 53·8; H, 5·4. $C_{31}H_{36}O_{10}NSBr$ requires C, 53·6; H, 5·2%), which had $[\alpha]_D^{22}$ = +42·0° in methyl alcohol (*c*, 0·4).

Resolution of (±)-*Hydrastine*-a.—(±)-Hydrastine-*a* hydrogen (+)-tartrate, prepared in alcoholic solution, crystallised from water in glistening silky needles, m. p. 110—111° (Hope, Pyman, Remfry, and Robinson, *loc. cit.*, give m. p. 108—110°), which had $[\alpha]_D^{25}$ = +6·6° in water (*c*, 0·4).

The (+)-camphor-10-sulphonate, prepared in aqueous solution, separated from water in glistening

white needles, m. p. 135—140°, with previous softening at 125° (Hope, Pyman, Remfry, and Robinson, *loc. cit.*, give m. p. 145° with sintering at 135°). Systematic fractional crystallisation of this *salt* (1·6 g.) from water yielded glistening colourless needles (0·6 g.), m. p. 120—122° after sintering at 110° (Found: C, 57·4; H, 6·3; H_2O, 5·4. $C_{31}H_{37}O_{10}NS,2H_2O$ requires C, 57·2; H, 6·3; H_2O, 5·5%), $[\alpha]_D^{15} = -25·4°$ in water (*c*, 1·3), unchanged by further crystallisation. The base (0·4 g.) liberated by addition of aqueous ammonia and isolated with methylene dichloride, had in the crude state $[\alpha]_D^{16} = +26·7°$ in chloroform (*c*, 0·2); crystallisation from methyl alcohol gave optically inactive (±)-hydrastine-*a* (0·2 g.), m. p. 138—139°, and (+)-*hydrastine*-a which separated from methyl alcohol in colourless prisms, m. p. 131—132° (Found: C, 65·8; H, 5·4. $C_{21}H_{21}O_6N$ requires C, 65·8; H, 5·5%), depressed to 127—128° when mixed with (±)-hydrastine-*a*. (+)-Hydrastine which had $[\alpha]_D^{19} = +42·2°$ in chloroform (*c*, 0·2) gave a *picrate* which separated from alcohol in glistening yellow needles, m. p. 185° (rapid heating, otherwise collapses at 155—160°) (Found: C, 52·3; H, 4·3; loss at 80°, 4·9%. $C_{27}H_{24}O_{13}N_4,CH_3·OH$ requires C, 52·2; H, 4·3; $CH_3·OH$, 5·0%).

Concentration of the (+)-camphor-10-sulphonate mother-liquors yielded a semi-solid mass which on basification gave a crude base (0·5 g.), $[\alpha]_D^{15} = -30·2°$ in chloroform (*c*, 0·25). After 2 crystallisations from methyl alcohol, (−)-hydrastine-*a* (0·4 g.) was obtained as glistening colourless prisms, m. p. 131—132° (Found: C, 66·1; H, 5·7%), depressed to 127—128° when mixed with (±)-hydrastine-*a*, but converted into (±)-hydrastine-*a*, m. p. 138—139°, by crystallisation from a methyl-alcoholic solution containing an equal weight of (+)-hydrastine-*a*, and giving no depression in m. p. when mixed with a specimen of naturally occurring (−)-hydrastine, m. p. 133°. (−)-Hydrastine-*a* had $[\alpha]_D^{14} = -42·1°$ in chloroform (*c*, 0·2) and under similar conditions naturally occurring (−)-hydrastine had $[\alpha]_D^{14} = -41·7°$. The *picrate* of synthetic (−)-hydrastine-*a* separated from alcohol in glistening yellow needles, m. p. 185° (rapid heating, otherwise collapses at 155—160°) (Found, in material dried at 80°: C, 53·2; H, 3·9. $C_{27}H_{24}O_{13}N_4$ requires C, 52·9; H, 3·9%), undepressed when mixed with the picrate prepared from natural (−)-hydrastine.

N-*Methyl*-N-(2-3′ : 4′-*dimethoxyphenylethyl*)*meconine-a-carboxyamide* (VII; R = Me), prepared as described for (VII; RR = CH_2), crystallised from methyl alcohol in glistening white prisms, m. p. 123—124° (Found: C, 63·7; H, 6·2. $C_{22}H_{25}O_7N$ requires C, 63·6; H, 6·0%).

Dehydrocordrastine (VIII; R = Me), prepared and isolated as described for dehydrohydrastine (VIII; RR = CH_2), was crystallised first from methyl alcohol and then from ethyl acetate; it formed orange-yellow prisms, m. p. 136—136·5° (Found: C, 66·2; H, 5·9. $C_{22}H_{23}O_6N$ requires C, 66·5; H, 5·8%).

Cordrastine I and Cordrastine II (I; R = Me).—Dehydrocordrastine (5 g.) was reduced in acetic acid (50 c.c.) as described in a similar case. Reduction was complete in 1 hour, and the product, isolated with methylene dichloride, was crystallised from methyl alcohol. *Cordrastine I* gradually separated in long, thin prisms (2·4 g.), m. p. 155—156° (Found: C, 66·4; H, 6·2. $C_{22}H_{25}O_6N$ requires C, 66·2; H, 6·3%). The *picrate* crystallised from methyl alcohol in stout yellow prisms, m. p. 153—154° (Found: loss in wt. at 90°, 1·4; C, 52·6; H, 4·5. $C_{28}H_{28}O_{13}N_4,\frac{1}{2}H_2O$ requires loss in wt., 1·4; C, 52·8; H, 4·6%).

The (+)-*camphor*-10-*sulphonate*, prepared in alcohol and precipitated by the careful addition of ether, crystallised from acetone in colourless, felted needles, m. p. 175—180° (Found: C, 61·2; H, 6·8. $C_{32}H_{41}O_{10}NS$ requires C, 60·9; H, 6·5%), $[\alpha]_D^{17} = +9·2°$ in water (*c*, 1·0). The (−)-*camphor*-10-*sulphonate*, prepared similarly, separated from acetone in felted needles, m. p. 175—180° (Found: loss in wt. at 100°, 1·4; C, 59·8; H, 6·6. $C_{32}H_{41}O_{10}NS,\frac{1}{2}H_2O$ requires loss in wt., 1·4; C, 60·0; H, 6·5%), $[\alpha]_D^{14} = -7·7°$ in water (*c*, 1·0). The (+)-*bromocamphor*-10-*sulphonate*, prepared from ammonium (+)-bromocamphor-10-sulphonate in aqueous solution, crystallised from methyl alcohol in elongated prisms, m. p. 215—218° (Found: C, 54·0; H, 5·6. $C_{32}H_{40}O_{10}NSBr$ requires C, 54·1; H, 5·6%), $[\alpha]_D^{17} = +34·8°$ in water (*c*, 1·1). The hydrogen (+)- and (−)-tartrates were uncrystallisable syrups.

A solution of picric acid (1·4 g.) in methyl alcohol (5 c.c.) was added to the hot methyl-alcoholic mother-liquors from which cordrastine-I had separated, and the picrate (3·3 g.) which separated on cooling was collected and refluxed with methyl alcohol (30 c.c.) for 30 minutes. The undissolved *cordrastine II picrate* (3·0 g.) was collected and crystallised from acetone in stout yellow rhombs, m. p. 202° (decomp.) with previous shrinkage at 165—170° (Found: C, 53·4; H, 4·6. $C_{28}H_{28}O_{13}N_4$ requires C, 53·5; H, 4·5%). Decomposition with methyl-alcoholic ammonia yielded *cordrastine II*, which crystallised from ether in colourless rhombic prisms, m. p. 118—119° (Found: C, 66·0; H, 6·3%). The *hydrogen* (−)-*tartrate*, prepared in alcohol, crystallised from methyl alcohol in clusters of slender colourless prism, m. p. 153—156° (Found: loss in wt. at 80°, 5·5; C, 56·0; H, 6·0. $C_{26}H_{31}O_{12}N,CH_3·OH$ requires loss in wt., 5·5; C, 55·8; H, 6·0%), $[\alpha] = {}_D^{14} -7·4°$ in water (*c*, 1·0).

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