76. *Studies of the Structure of Emetine. Part V.* The Structure of the Rubremetinium Salts.*

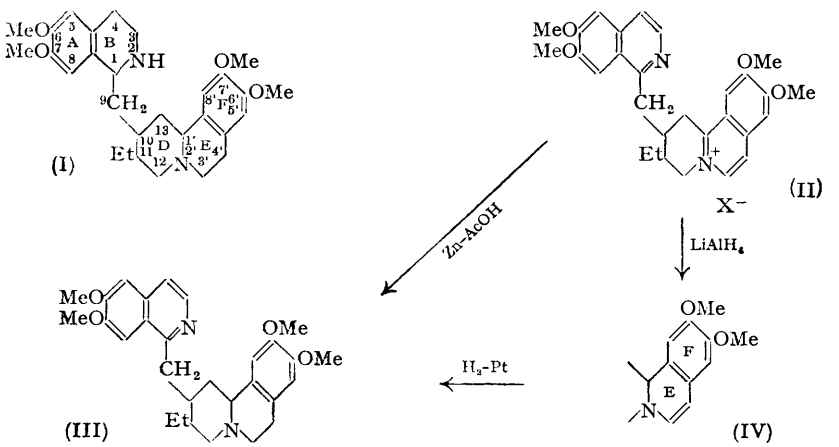
By H. T. Openshaw and H. C. S. Wood.

Catalytic hydrogenation of rubremetinium chloride produces two stereoisomeric dihydrorubremetines, which exhibit pyrrole colour reactions and are readily re-oxidised to rubremetinium chloride. The constitution of the rubremetinium salts is discussed in the light of these observations, of their previously described reactions, and of the course of the dehydrogenation of emetine, and it is concluded that they are most adequately represented by the structure (V) (Battersby, Openshaw, and Wood, *Experientia*, 1949, **5**, 114). The structures of *O*-methylpsychotrine and tetradehydroemetine are also discussed, that of the former being revised to (VII).

The establishment of the structure (I) for emetine necessitates a reconsideration of the constitution of the highly coloured rubremetinium salts, which are formed by treating the alkaloid with mild acidic oxidising agents such as ferric chloride, bromine, iodine, or mercuric acetate (Carr and Pyman, *J.*, 1914, **105**, 1591; Karrer, *Ber.*, 1916, **49**, 2057; Battersby and Openshaw, Part II, *J.*, 1949, S 67). The reaction involves the removal of eight hydrogen atoms and the formation of a salt of a monoacidic, quaternary base, according to the equation :

$$C_{29}H_{40}O_4N_2 - 8H + HX = C_{29}H_{33}O_4N_2X$$

Three different structures have been put forward for these salts.† The first, due to Brindley and Pyman (*J.*, 1927, 1067), was based on an incorrect emetine formula and need



not be considered further. The second was proposed by Karrer, Eugster, and Rüttner (*Helv. Chim. Acta*, 1948, **31**, 1219), who considered that the oxidation involves the aromatis-

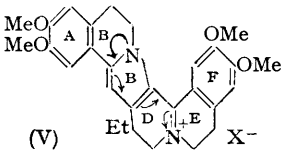
* Part IV, *J.*, 1949, 3207.

† Pyman designated these substances as salts of a hypothetical anhydro-base, $C_{29}H_{32}O_4N_2$, which he named " rubremetine "; it is convenient to retain this name as a generic term for the rubremetinium salts. Karrer preferred the name " dehydroemetine."

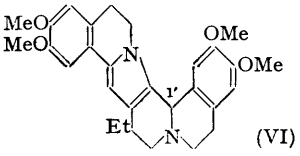
ation of rings B and E, leading to the structure (II). This suggestion was based largely on the reduction of rubremetine by zinc and acetic acid to a crystalline, optically active tetrahydro-derivative which was resistant to catalytic hydrogenation. This behaviour was ascribed to the known ease of reduction of a quaternary *iso*quinolinium system (ring E) and the contrasting resistance to reduction of a non-quaternised *iso*quinoline (ring B); the reduction product was assigned the structure (III). Since this structure had already been assigned to the minor alkaloid emetamine, the tetrahydro-compound was assumed to be a stereoisomer of emetamine. On this view, it would be expected that emetamine should also yield rubremetine on oxidation. However, Karrer, Eugster, and Rüttner confirmed, by absorption-spectrum measurements, the earlier statement of Brindley and Pyman (*loc. cit.*) that the oxidation product of emetamine, although coloured and quaternary, is not identical with rubremetine. This observation, and the failure of the structure (II) to account for the lack of basicity of the non-quaternary nitrogen atom and for the intense colour of the salts, seem to provide sufficient grounds for the rejection of the Karrer proposal.

Recently, however, Karrer and Rüttner (*Helv. Chim. Acta*, 1950, **33**, 291) have brought forward further evidence which they consider to indicate the presence in rubremetine of a quaternary *iso*quinolinium system. On treatment with lithium aluminium hydride, rubremetinium bromide yielded a crystalline, very unstable compound analysing as a dihydrorubremetine, $C_{29}H_{34}O_4N_2$. By analogy with the similar reduction of simple *iso*quinolinium salts this product was assigned the partial structure (IV). On catalytic hydrogenation it absorbed one mol. of hydrogen to give a mixture of two supposed tetrahydrorubremetines, one of which was identical with that obtained by zinc dust reduction of rubremetine. The second product was characterised by an exceptionally large lævorotation ($[\alpha]_D$ −380°); both products had identical ultra-violet absorption spectra.

In an attempt to overcome the various objections to the structure (II), Battersby, Openshaw, and Wood (*Experientia*, 1949, **5**, 114) advanced an alternative, mesomeric structure (V), which is similar to that of a cyanine dye, the single positive charge being



(V)

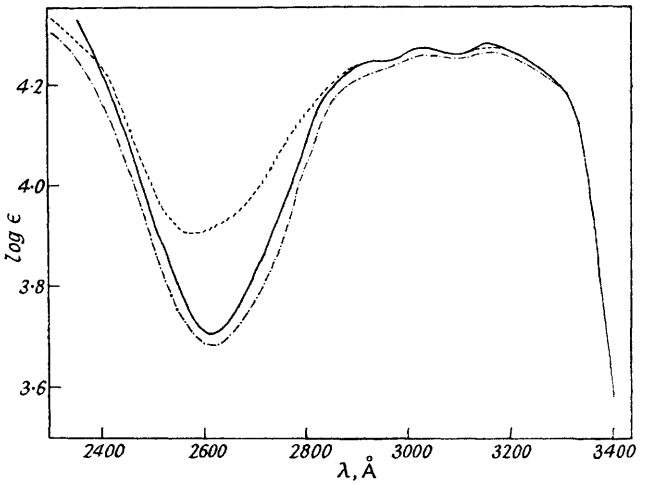


(VI)

shared between the two nitrogen atoms. This structure is consistent with the intense colour of the substance, with its behaviour as a monoacidic, quaternary base, and with the formation of a different product by the oxidation of emetamine. The structure (V) contains a pyrrole nucleus and we found that the crude product of zinc dust reduction of rubremetine gives pyrrole colour reactions. A further study of the reduction of rubremetine has provided additional support for the structure (V).

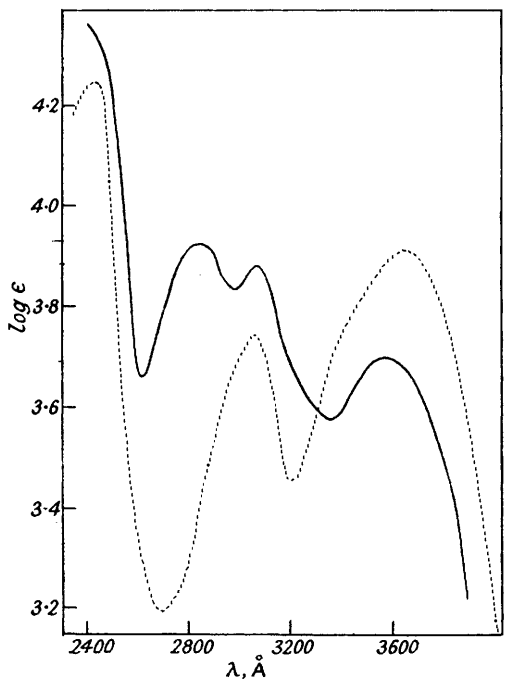
On hydrogenation of rubremetinium chloride in ethanol, in the presence of sodium acetate and platinic oxide, 1·0 mol. of hydrogen is absorbed and the solution becomes colourless. Although the product is readily re-oxidised by air in the presence of the catalyst (Part II, *loc. cit.*), it is relatively stable when the platinum is removed. It consists of a mixture of two stereoisomeric dihydrorubremetines, the α-isomer being strongly lævorotatory ($[\alpha]_D$ −395°) and the β-isomer even more strongly dextrorotatory ($[\alpha]_D$ +406°). When the original mixture is crystallised from methanol, a partial racemate separates as a very sparingly soluble methanol complex containing one molecule of each isomer and two molecules of methanol, and having m. p. 128° and $[\alpha]_D$ +21°. From the mother-liquor, the pure α-isomer (m. p. 198°) is obtained. The complex splits up on crystallisation from ethanol, and the less soluble β-isomer (m. p. 202°) separates first. If methanol solutions of the two pure isomers are mixed, the partial racemate is again precipitated. The relation between these two isomers thus resembles very closely that of a pair of enantiomorphs; they have opposite and nearly equal rotations, they have

FIG. 1.



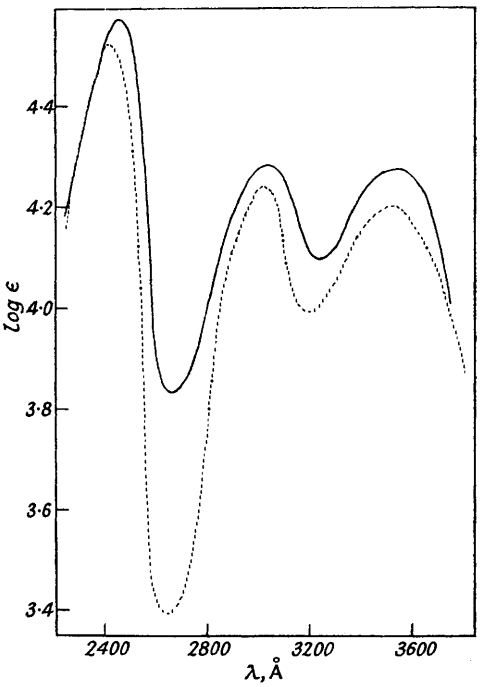
——————— *α-Dihydrorubremetine in methanol.*
– – – – – – – – – *β-Dihydrorubremetine in methanol.*
— · — · — · — *"Tetrahydro- and* isotetrahydro-*dehydroemetine"* (*Karrer and Rüttner*).

FIG. 2.

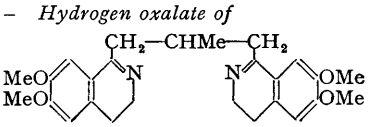


——— O-*Methylpsychotrine hydrogen oxalate in ethanol.*
– – – – *Hydrochloride of* 3 : 4-*dihydro*-1-*methyl*-6 : 7-*methylenedioxy- or* 1-*benzyl*-3 : 4-*dihydro*-6 : 7-*methylenedioxy*-isoquinoline *in ethanol* (*Bills and Noller*).

FIG. 3.



——— *Tetradehydrometine hydrogen oxalate in water.*
– – – – *Hydrogen oxalate of*

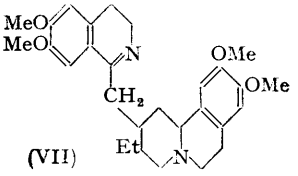


in water (*McIntyre, Openshaw, and Wood*).

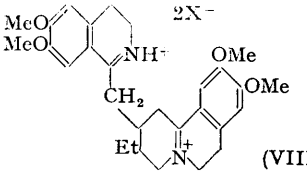
nearly equal melting points, and they form a molecular complex analogous to a racemate. However, they differ sufficiently in solubility to admit of their separation.

Both the isomeric dihydrorubremetines exhibit the pine-shaving reaction, give a green colour with Ehrlich's reagent, and couple with sodium diazobenzene-*p*-sulphonate; emetine shows none of these reactions. Potentiometric titration shows them to be monoacidic bases. They possess almost identical absorption spectra (Fig. 1). They resist further hydrogenation, and on oxidation with mercuric acetate are reconverted into rubremetine. These properties are consistent with the structure (VI), the formation of two stereoisomers being due to the formation of a new asymmetric centre ($C_{(1')}$) in the reduction.

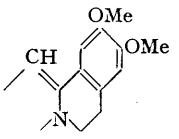
Some support for the structure (V) for rubremetine can also be gained by a consideration of the course of oxidation of emetine. Most of the oxidising agents used are known to be capable of converting a tetrahydro- into a 3 : 4-dihydro-*iso*quinoline. Pyman (*J.*, 1917, **111**, 419) showed that the first oxidation product is *O*-methylpsychotrine, which he formulated as a 1 : 9-dehydroemetine. Bills and Noller (*J. Amer. Chem. Soc.*, 1948, **70**, 957) have shown, however, that the 1 : 2-position of the double bond is strongly favoured in 1-substituted 3 : 4-dihydro*iso*quinoline derivatives. We have therefore measured the ultra-violet absorption spectrum of *O*-methylpsychotrine (Fig. 2) and find that it corresponds with the structure (VII), since it shows maxima corresponding both to those of the 3 : 4-dihydro*iso*quinoline system (rings A and B) and to those of the tetrahydro*iso*-



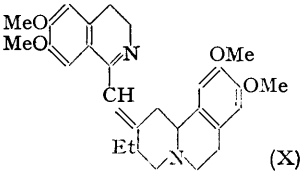
(VII)



(VIII)



(IX)



(X)

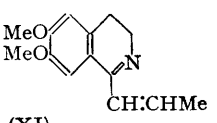
quinoline system (rings E and F) (cf. Part I, *J.*, 1949, S 59). Battersby and Openshaw (Part II, *loc. cit.*) isolated the base tetradehydroemetine as the product of the second stage of the oxidation. The structure of this substance is still uncertain. Its salts are reasonably stable, and the most natural assumption is that they possess the structure (VIII); the ultra-violet absorption spectrum is consistent with the presence of two 3 : 4-dihydro*iso*quinoline nuclei (Fig. 3).* The free base, which would in this case possess the alternative double bond arrangement (IX), is much less stable, as would be expected from the work of Bills and Noller (*loc. cit.*).

Doubt is cast on the correctness of the structure (VIII), however, by certain observations by Hazlett and McEwen (*J. Amer. Chem. Soc.*, 1951, **73**, 2578), who have reinvestigated the mercuric acetate oxidation of emetine, with results differing in some respects from ours. They obtained, in addition to tetradehydroemetine (32%), an approximately equal quantity of a more stable, isomeric base, *iso*tetradehydroemetine (28% yield). The formation of this new isomer must be ascribed to some difference in reaction conditions, since we have never encountered it in the numerous oxidations we have carried out, in spite of a careful search for other products, and in recent experiments approximately 90% of the original emetine has been accounted for as tetradehydroemetine or rubremetine. That the new base cannot be merely a stereoisomer of (VIII), differing from tetradehydroemetine in the configuration of one or both the remaining asymmetric centres ($C_{(10)}$ and $C_{(11)}$), is shown by the formation of emetine from both isomers by hydro-

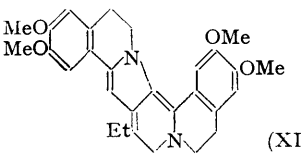
* Redetermination shows that the values of the extinction coefficients given in Part II are too low, but the positions of the maxima are substantially confirmed.

genation. We have obtained only *iso*emetine (isolated in 78% yield as the benzoyl derivative) by the hydrogenation of an aqueous solution of tetradehydroemetine hydrogen oxalate, but Hazlett and McEwen, using an alcoholic suspension of the salt, obtained a little emetine and *iso*emetine, and much larger amounts of two new stereoisomers of emetine; hydrogenation of *iso*tetradehydroemetine gave emetine as the only isolable product. The very close similarity of the absorption spectra of the two isomeric tetradehydroemetines makes it unlikely that they differ in the positions of their double bonds, and the foregoing observations are most readily interpreted by formulating the two bases as the *cis*- and the *trans*-isomer of a conjugated structure (X) similar to that proposed in Part II. The remarkably close correspondence of their absorption spectra with that of a synthetic bis-3 : 4-dihydro*iso*quinoline (Fig. 3) must then be dismissed as fortuitous, however. An attempt to synthesise 3 : 4-dihydro-6 : 7-dimethoxy-1-propenyl*iso*quinoline (XI) for spectral comparison has so far failed in its object, as it has not been found possible to purify the product owing to its instability.

No further intermediate stages in the oxidation of emetine to rubremetine have been isolated, but it is possible that the next step involves attack on $C_{(13)}$, which is activated either by the $C{=}N^+$ group (structure VIII) or by the conjugated system (structure X); removal of a hydrogen atom and an electron would be followed by cyclisation, giving respectively a dihydropyrrole derivative or dihydrorubremetine (VI), either being readily dehydrogenated to rubremetine.



(XI)



(XII)

The structure (V) for rubremetine has been criticised by Karrer and Rüttner on the grounds that it contains two dihydropyridine rings (D and E) which should be highly susceptible to oxidation. Ring E, however, as represented in structure (V), forms part of a 3 : 4-dihydro*iso*quinoline system, the stability of which is well known. Dehydrogenation of such a structure cannot normally be achieved by the action of halogens (see, for example, Leonard and Leubner, *J. Amer. Chem. Soc.*, 1949, **71**, 3408), and we have found that hot aqueous mercuric acetate is also ineffective. Ring D is fused to a pyrrole ring and thus forms a system not unlike that present in the alkaloid harmaline; moreover, the molecule probably gains additional stability from its resonance-hybrid character.

Karrer and Rüttner also consider that the structure (V) is inconsistent with their observations on the reduction of rubremetine with lithium aluminium hydride. It should, however, be pointed out that their interpretation of this reaction is open to question. Reduction of (II) to the dihydro-derivative (IV) introduces a new asymmetric centre, but only one crystalline product was isolated. The further hydrogenation of this apparently homogeneous product gave rise to two stereoisomeric tetrahydro-compounds, although no new asymmetric centre is formed in this reaction. It may be significant that these two products have absorption spectra identical with that of α-dihydrorubremetine (Fig. 1), and that one of them ("*iso*tetrahydrodehydroemetine") resembles this substance also in its melting point and in its exceptionally high lævorotation. The analytical figures given for this product also agree more closely with those of a dihydrorubremetine.

Hazlett and McEwen (*loc. cit.*) have obtained an optically inactive base having an absorption spectrum similar to that of dihydrorubremetine, by the hydrogenation of an unstable, crystalline "dehydrohalorubremetine" produced by treatment of rubremetinium chloride with alkali. Although they designate this product as a tetrahydro-compound, they admit that this designation is insecurely based, since the hydrogenation was carried out on crude material. It seems probable to us that the substance is a racemic dihydrorubremetine (VI) and that the dehydrohalorubremetine from which it is derived has the structure (XII), in which the sole remaining asymmetric centre of rubremetine has been destroyed.

It thus appears to us that the majority of the properties and reactions of the rubremetinium salts can be best explained on the basis of structure (V). Since this structure contains only one asymmetric centre ($C_{(11)}$) whereas emetine contains four, the rubremetinium salts should prove convenient transformation products through which synthetic ipecacuanha alkaloids of unknown or mixed stereochemical configuration may be compared with the natural materials. (±)-Rubremetinium bromide has already been obtained (Battersby and Openshaw, *Experientia*, 1950, **6**, 378) by the dehydrogenation of a synthetic base of structure (VII), and in order to facilitate the eventual resolution of such a product, we have prepared some diastereoisomeric salts of (+)-rubremetine.

Experimental

(M. p.s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford. Absorption spectra were measured on a " Unicam " S.P. 500 Spectrophotometer.)

Mercuric Acetate Oxidation of Emetine.—The original procedure (Part II, *loc. cit.*) has been slightly modified to increase the total yield of oxidation products. A solution of mercuric acetate (61·9 g.), potassium acetate (6·2 g.), and acetic acid (25 ml.) in water (550 ml.) was added during 1 hour to a hot solution of emetine hydrochloride heptahydrate (20 g.) in water (240 ml.); the mixture was heated for a further 2 hours at 100°, cooled, filtered from mercurous acetate, and freed from dissolved mercury salts with hydrogen sulphide as described previously. The combined filtrate and washings were concentrated to 400 ml., treated with concentrated hydrochloric acid (20 ml.), and cooled slowly, whereupon the bulk of the rubremetinium chloride crystallised. The filtrate was made strongly alkaline with sodium carbonate and extracted five times with ether; the residue left on evaporation of the ether was treated with alcoholic oxalic acid, tetradehydroemetine hydrogen oxalate (8·95 g., 43%), m. p. 153—154°, crystallising immediately. The aqueous solution remaining after the ether-extraction was acidified with hydrochloric acid and evaporated to dryness, and the residue was extracted with acetone and alcohol. The extracts yielded, on evaporation and crystallisation from water, a further quantity of rubremetinium chloride (total, 8·28 g.; 46%).

The specific rotation of rubremetinium chloride was measured, for an air-dried sample containing 5·85% of water; the values are calculated for the anhydrous material: $[\alpha]_D^{15}$ +52·0°, $[\alpha]_{5461}^{15}$ +25·4° (*c*, 0·4 in water).

Hydrogenation of Rubremetinium Chloride.—A solution of the salt (4·0 g.) and sodium acetate trihydrate (3·5 g.) in ethanol (55 ml.) was shaken with hydrogen and platinic oxide (0·15 g.), rapid absorption of 1 mol. of hydrogen occurring. The filtered, pale yellow solution gave $[\alpha]_D^{17}$ −140° and on evaporation left a gum which was suspended in excess of sodium hydroxide solution and extracted with ether. The extracts, on evaporation and crystallisation from ethanol, gave a mass of pale yellow needles, m. p. 173—178° (3·5 g., 88%). On treatment with hot methanol (100 ml.) a portion of the material remained undissolved; it was collected and recrystallised several times from a larger volume of methanol, until the m. p. and rotation were constant. The resulting *complex*, containing one molecule each of α- and β-dihydrorubremetine and two molecules of methanol, formed fine colourless prisms, m. p. 127—128° (with sintering from 125°), $[\alpha]_D^{18}$ +21·2° (*c*, 0·176 in acetone) (Found: C, 71·1; H, 7·5. $2C_{29}H_{34}O_4N_2,2CH_3{\cdot}OH$ requires C, 71·2; H, 7·5%). The complex was decomposed by crystallisation several times from ethanol, the less soluble isomer, *β-dihydrorubremetine*, separating as very fine, feathery needles, m. p. 201—202°, $[\alpha]_D^{16}$ +406·3° (*c*, 0·148 in acetone) (Found: C, 73·5; H, 6·8; N, 6·1. $C_{29}H_{34}O_4N_2$ requires C, 73·4; H, 7·2; N, 5·9%).

The original methanol filtrate was concentrated to 50 ml. and, on its cooling, *α-dihydrorubremetine* crystallised; after repeated crystallisation from methanol it formed colourless needles, m. p. 197—198°, $[\alpha]_D^{15}$ −395° (*c*, 0·165 in acetone) (Found: C, 73·1; H, 7·4; N, 6·0%). Potentiometric titration (" Marconi " pH meter and glass electrode) of a solution of α-dihydrorubremetine in excess of aqueous-alcoholic hydrochloric acid against 0·1N-sodium hydroxide showed the substance to be a monoacidic base (Found: equiv., 457. Calc. for $C_{29}H_{34}O_4N_2$: equiv., 474).

Colour Reactions of the Dihydrorubremetines.—The two isomers gave identical results in the following reactions: (*a*) A bright carmine colour was imparted to a pine shaving moistened with hydrochloric acid and held in the vapour from the destructive distillation of dihydrorubremetine. (*b*) A trace of dihydrorubremetine, dissolved in ethanol, was treated with a drop of Ehrlich's *p*-dimethylaminobenzaldehyde reagent. An intense green colour was produced, which became red on addition of excess of reagent. (*c*) A solution of dihydrorubre-

metine in dilute acetic acid was treated with a solution of sodium diazobenzene-*p*-sulphonate. A brilliant red azo-dye was produced. Emetine hydrochloride and tetradehydroemetine hydrogen oxalate gave no colour under these conditions.

Mercuric Acetate Oxidation of the Dihydrorubremetines.—α-Dihydrorubremetine (0·1 g.), in dilute acetic acid (2 ml.), was treated with a solution of mercuric acetate (0·148 g.), potassium acetate (0·025 g.), and acetic acid (0·2 ml.) in water (3 ml.), and the mixture was heated under reflux at 110—120° (bath) for 3½ hours. When isolated in the usual manner, rubremetinium chloride (0·028 g., 21% calc. as hexahydrate) was obtained as scarlet needles, m. p. (air-dried) 126—127° (decomp.) both alone and in admixture with an authentic specimen of m. p. 121—123°. β-Dihydrorubremetine gave an identical yield of air-dried material, m. p. and mixed m. p. 123—125° (decomp.).

Attempted Oxidation of 3 : 4-*Dihydro*isoquinolines *with Mercuric Acetate.*—(With Dr. A. R. Battersby.) 1-*n*-Butyl-3 : 4-dihydro*iso*quinoline (0·516 g.) was mixed with a solution of mercuric acetate (1·81 g.), potassium acetate (0·1 g.), and acetic acid (0·5 g.) in water (15 ml.) and heated under reflux for 7 hours. On cooling, there was a very slight deposit of mercurous acetate (90 mg.), which was removed. The filtrate was freed from mercury salts with hydrogen sulphide, and the resulting solution was made strongly alkaline with sodium hydroxide and extracted three times with ether, each ethereal extract being washed once with water. The combined extracts were dried and evaporated, to give a yellow oil (0·490 g.). A portion (0·22 g.) of this was converted into the picrate (0·44 g.), which formed yellow plates, m. p. 152—153°, undepressed on admixture with 1-*n*-butyl-3 : 4-dihydro*iso*quinoline picrate (m. p. 152—153°).

No reaction occurred when 3 : 4-dihydro-6 : 7-dimethoxy-1-methyl*iso*quinoline (1 g.) was heated under reflux for 4 hours with a solution of mercuric acetate (3·5 g.) and acetic acid (1 ml.) in water (10 ml.).

Hydrogenation of Tetradehydroemetine.—A solution of tetradehydroemetine hydrogen oxalate (1·0 g.) in water (30 ml.) was shaken with hydrogen and platinic oxide (0·1 g.) at room temperature and pressure; 2·0 mols. of hydrogen were absorbed in 40 minutes. After removal of the catalyst, the solution was evaporated to dryness under reduced pressure. The residual yellow gum (0·95 g.) was dissolved in water and treated with hydrobromic acid (15 ml. of 2N.), but no emetine hydrobromide separated even after seeding. The base (0·72 g.) was recovered, dissolved in ether, mixed with benzoic anhydride (0·15 g.), and heated on the steam-bath for 45 minutes, the ether being allowed to evaporate. The product was worked up according to the directions of Pyman (*loc. cit.*), and benzoyl*iso*emetine (0·67 g., 78%) was obtained as white hexagonal prisms, m. p. 201—202°. One recrystallisation from acetone raised the m. p. to 202—203°; $[\alpha]_D^{17}$ was +48·0° (*c*, 2·0 in chloroform). Pyman gives m. p. 207—208° (corr.) and $[\alpha]_D$ +48·9°. No other reduction products could be isolated.

Tetradehydroemetine base (0·75 g.) (recovered from the hydrogen oxalate), dissolved in ethanol (40 ml.) and shaken with hydrogen and platinic oxide (0·1 g.), absorbed 2·0 mols. of hydrogen. On treatment of the product as described above, benzoyl*iso*emetine (0·146 g., 36%) was the sole crystalline material isolated.

Attempted Synthesis of 3 : 4-*Dihydro*-6 : 7-*dimethoxy*-1-*propenyl*isoquinoline (XI).—2-(3 : 4-Dimethoxyphenyl)ethylamine (4·13 g.), dissolved in anhydrous ether (60 ml.), was treated dropwise with a solution of crotonyl chloride (1·3 g.) in anhydrous ether (40 ml.) with continuous shaking, a white precipitate being formed. After being left for several days, the mixture was treated with water (40 ml.), whereupon the precipitate dissolved and large yellow needles (1·74 g.) of the amide, m. p. 82—84°, separated from the aqueous phase. After the collection of this material, the aqueous layer was saturated with ammonium sulphate and the ethereal layer was separated. The aqueous layer was extracted thrice with ether, and the combined ethereal solutions on evaporation and crystallisation of the residue from water gave a further crop (1·1 g.; total, 98%) of crystalline amide, m. p. 84—85°. After recrystallisation twice from water the substance had m. p. 85—86°.

Phosphoric oxide (2·5 g.) was added to a solution of the foregoing amide (1 g.) in anhydrous toluene (20 ml.), and the mixture was refluxed for 10 minutes, the phosphoric oxide becoming yellow and sticky. A second portion of phosphoric oxide (2·5 g.) was then added and, after 15 minutes' refluxing, a third portion (2·0 g.); finally, the mixture was refluxed for 20 minutes, cooled, and treated cautiously with water (20 ml.), followed by hydrochloric acid (10 ml. of 2N.). After thorough shaking, the toluene layer was removed and extracted with two further portions of dilute hydrochloric acid, and the combined acid extracts were basified and extracted with ether. The ethereal extract, which became cloudy on exposure to air and darkened appreciably, was dried and evaporated, leaving the dihydro*iso*quinoline (XI) as a yellowish-

red gum (0·87 g., 94%) which would not crystallise. No crystalline hydrobromide, hydrogen oxalate, or picrate could be obtained. Solutions of the base or its salts darkened rapidly on exposure to air and light, forming resinous substances. Distillation of a sample of the base at 190° (bath)/2 × 10^{-5} mm. gave a dark brown, resinous distillate, and a large residue which polymerised to a hard black resin.

Diastereoisomeric Rubremetinium Salts.—Hot aqueous solutions of rubremetinium chloride (0·2 g. in 2 ml.) and sodium (+)- or (−)-camphor-10-sulphonate (0·88 g. in 1 ml.) were mixed; on cooling, the product crystallised in red leaflets (0·21 g., 92%) and was recrystallised from water (10 ml.). (+)-Rubremetinium (+)-camphor-10-sulphonate had m. p. 183—184° (decomp.); the (−)-camphor-10-sulphonate had m. p. 176—177° (decomp.). The two salts did not differ appreciably in solubility; they were readily soluble in ethanol and acetone, soluble in hot water, and almost insoluble in ethyl acetate.

The α-bromocamphor-π-sulphonates were prepared in a similar manner, with 0·1 g. of ammonium (+)- or (−)-α-bromocamphor-π-sulphonate; in each case the product formed orange-red leaflets (0·255 g., 100%). (+)-Rubremetinium (+)-bromocamphorsulphonate, crystallised from water (15 ml.), had m. p. 239° (sintering at 237°); it was noticeably less soluble than the (−)-bromocamphorsulphonate, which after crystallisation from water (10 ml.) had m. p. 217° (sintering at 213°). Both salts were readily soluble in ethanol and acetone and almost insoluble in ethyl acetate.

We are grateful to the Wellcome Foundation Limited for generous gifts of emetine, and to Imperial Chemical Industries Limited for grants and for the loan of the spectrophotometer. One of us (H. C. S. W.) acknowledges with thanks the receipt of a Maintenance Award from the Department of Scientific and Industrial Research.

UNITED COLLEGE, UNIVERSITY OF ST. ANDREWS. [*Received, August 27th*, 1951.]