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# 1,2-DIHYDROISOQUINOLINES—IV[1]

## ACYLATION

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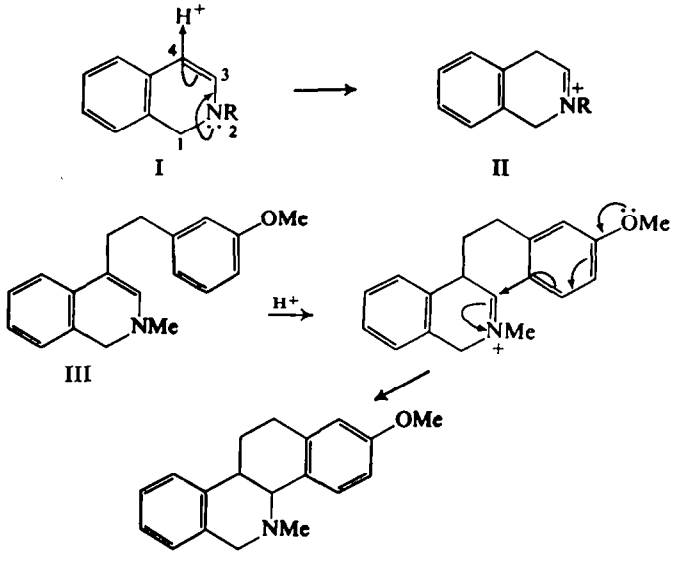
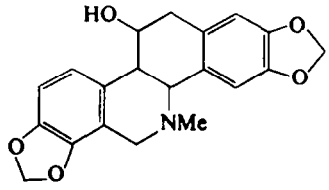
**Abstract**—By reacting 2-methyl-1,2-dihydroisoquinoline with acid chlorides the $C_4$-acylated 1,2-dihydroisoquinoline, and the corresponding 4-acylisocarbostyril are formed. Some properties of representative members of each class of product are described.

WHEN a 1,2-dihydroisoquinoline (I) is treated with mineral acid, the $C_4$-protonated form (II) is susceptible to nucleophilic attack at $C_3$, and examples of such reactions are provided by the formation of pavine from 1,2-dihydropapaverine,[2] the rearrangement of 1-benzyl-1,2-dihydroisoquinolines to the 3-benzyl-3,4-dihydroisoquinoline derivatives[3,4] and the formation of the berberine skeleton from the N-$\beta$-arylethyl-1,2-dihydroisoquinolines.[5–7] It occurred to us that a synthesis of the benzo[c]phenanthridine ring system (IV) may be achieved from a suitable 1,2-dihydro-

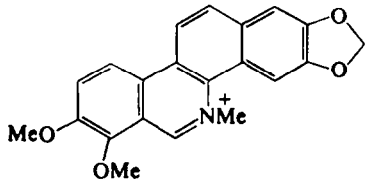



[1] Part III. D. W. Brown and S. F. Dyke, *Tetrahedron* **22**, 2437 (1966).
[2] A. R. Battersby and R. Binks, *J. Chem. Soc.* 2888 (1955).
[3] J. Knabe and J. Kubitz, *Angew. Chem.* (Int. Ed.) **2**, 689 (1963); *Arch. Pharm.* **297**, 129 (1964); J. Knabe and N. Ruppenthal, *Ibid.* **297**, 141, 268 (1964); *Naturwiss.* 482 (1964).
[4] S. F. Dyke and M. Sainsbury, *Tetrahedron Letters* 1545 (1964); *Tetrahedron* **21**, 1907 (1965).
[5] J. W. Huffman and E. G. Miller, *J. Org. Chem.* **25**, 90 (1960).
[6] A. R. Battersby, D. J. Le Count, S. Garratt and R. I. Thrift, *Tetrahedron* **14**, 46 (1961).
[7] D. W. Brown and S. F. Dyke, *Tetrahedron Letters* 3587 (1964); 1,2-Dihydroisoquinolines Part II, *Tetrahedron* **22**, 2429 (1966).

isoquinoline of the type III. The benzo[c]phenanthridine ring system is found in a few alkaloids,[8] the two main types being exemplified by chelidonine (V) and chelerythrine (VI). Syntheses of some of the fully aromatic members have been reported,[9] but the position of the hydroxyl group in alkaloids such as V, although in little doubt, has not been confirmed. Very little other synthetic work in the



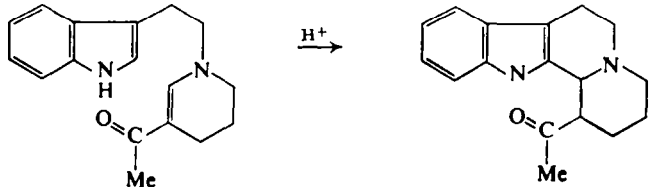

V



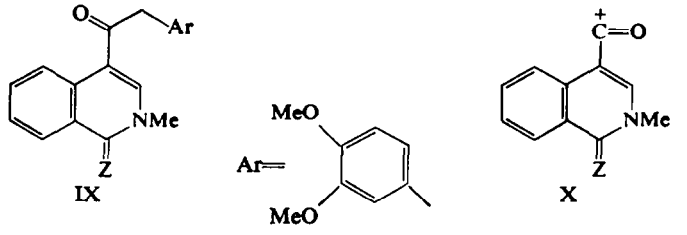

VI

benzo[c]phenanthridine series has been successful; some aspects have been briefly reviewed[10] and some other attempts described.[10] Our interest in this group of alkaloids was aroused by their possible biological activity, and we hoped to devise a more flexible synthesis than any of these previously reported. Although we have so far been unable to achieve a new synthesis of the benzo[c]phenanthridine skeleton, we wish to report here the preparation and some chemistry of potential intermediates.

4-Alkylisoquinoline derivatives can be prepared by the ring-closure of β-alkyl-β-aryl-ethylamines, but we decided to take advantage of the known enamine character of 1,2-dihydroisoquinoiines, and to prepare the model compound (IX, Z = $H_2$) by the interaction of 2-methyl-1,2-dihydroisoquinoline and 3,4-dimethoxyphenylacetyl chloride. We were encouraged by the report[11] that the vinylogous amide (VII) was readily ring-closed by molar hydrochloric acid solution to VIII. Since the commencement of this work, Grewe *et al.*[12] reported that 4-β-phenylethyl-1,2,3,4-




VII VIII




IX X

[8] R. H. F. M. Manske and H. L. Holmes, *The Alkaloids* Vol. IV; Chap. 35, Academic Press, New York (1954); R. H. F. Manske, *The Alkaloids* Vol. VII, p. 430, Academic Press, New York (1960).

[9] A. S. Bailey and C. R. Worthing, *J. Chem. Soc.* 4535 (1956) and Refs therein; H. R. Arthur and Y. L. Ng, *Ibid.* 4010 (1959); K. W. Gopinath, T. R. Govindachari, P. C. Parthasarathy and N. Viswanathan, *Ibid.* 4012 (1959).

[10] R. A. Abramovitch and G. Tertzakian, *Canad. J. Chem.* **41**, 2265 (1963).

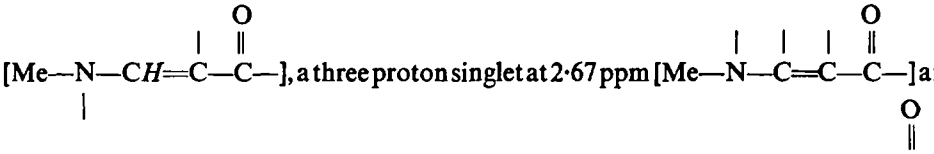
[11] E. Wenkert and B. Wickberg, *J. Amer. Chem. Soc.* **87**, 1580 (1965).

[12] R. Grewe, W. Kruger and E. Vangermain, *Chem. Ber.*, **97**, 119 (1964).

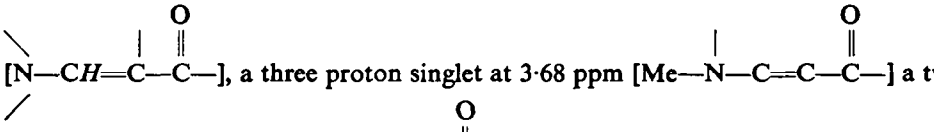
tetrahydroisoquinoline is formed by the reductive alkylation of isoquinoline with phenylacetaldehyde, but this reaction was subsequently shown[1] to yield the corresponding N-β-phenylethyltetrahydroisoquinoline instead. Bobbitt *et al.*[13] have described the preparation of 4-benzylisoquinolines by the interaction, in acid solution, of benzaldehyde and various 1,2-dihydroisoquinolines.

When equivalent amounts of 2-methyl-1,2-dihydroisoquinoline and 3,4-dimethoxyphenylacetyl chloride were allowed to react, in a nitrogen atmosphere, in benzene solution containing one equivalent of triethylamine, three neutral, nitrogenous products were isolated. The first compound, m.p. 116–118° was shown, as indicated below, to be the expected vinylogous amide (IX, $Z = H_2$); the second product, m.p. 167–168° was the related isocarbostyril (IX, Z = O) and the third proved to be 2-methylisocarbostyril. When a benzene solution of IX ($Z = H_2$) is exposed to air, or when it is treated in acetone with active manganese dioxide, the isocarbostyril (IX, Z = O) is formed. The latter compound could conceivably arise, in the acylation reaction, by acylation of some preformed 2-methylisocarbostyril, but this was shown not to be the case.

The base-peak in the mass spectrum[14] of IX ($Z = H_2$) occurs at *m/e* 172, corresponding to the fragment X ($Z = H_2$), which arises by the expected loss of the 3,4-dimethoxybenzyl group. Similarly, the base-peak in the mass spectrum of IX (Z = O) occurs at *m/e* 186, corresponding to the ion X (Z = O). The IR spectrum of IX ($Z = H_2$) in chloroform exhibits peaks at 1625 $cm^{-1}$ and 1580 $cm^{-1}$ [>C=C< and >C=O groups], whereas the IR spectrum of IX (Z = O) shows a band at 1645 $cm^{-1}$, characteristic of the carbonyl group in an isocarbostyril. IR carbonyl frequencies as low as 1563 $cm^{-1}$ have been reported[15] for some enamino ketones. The NMR spectrum[16] of IX ($Z = H_2$) in $CDCl_3$ shows a one proton singlet at 7·5 ppm



two proton singlets at 4·45 ppm and 3·88 ppm [Ar—$CH_2$—N<] and [Ar—$CH_2$—C—]. The NMR spectrum of IX (Z = O) exhibited a one proton singlet at 8·13 ppm



proton singlet at 4·15 ppm [Ar—$CH_2$—C—] and a one proton multiplet at 9·02 ppm [characteristic of the $C_8$-H in an isocarbostyril]. The NMR spectra of vinylogous amides have been discussed in the literature.[17]

[13] J. M. Bobbitt, D. P. Winter and J. M. Kiely, *J. Org. Chem.* **30**, 2459 (1965).

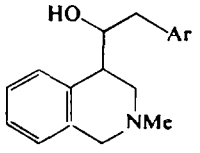
[14] Recorded on the A. E. I. MS9 Mass Spectrometer at the University of Sheffield. We are indebted to Dr. C. P. Falshaw for the measurement and discussion of the mass spectra of IX ($Z = H_2$) and (Z = O).

[15] G. O. Dudek, *J. Org. Chem.* **30**, 548 (1965).

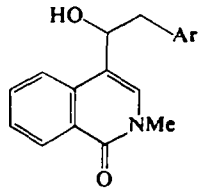
[16] NMR spectra were measured with a Varian A.60 spectrometer. Chemical shifts positions are measured in ppm downfield from TMS used as an internal standard.

[17] D. L. Ostercamp, *J. Org. Chem.* **30**, 1169 (1965).

Reduction of either IX (Z = $H_2$ or Z = O) with LAH gave the same saturated alcohol (XI), characterized as its O-acetyl methiodide. Other examples are known[18] of the reduction of enamino ketones to saturated alcohols by this reagent. The same alcohol (XI) was produced by reducing IX (Z = $H_2$) with sodium borohydride. When, however, IX (Z = O) was treated with this reagent, the allylic alcohol (XII) was formed. The hydroxyl group of IX is remarkably unreactive; no oxidation




XI

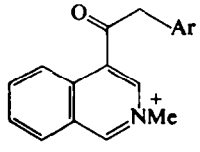



XII

occurred when it was treated with aluminium t-butoxide and benzophenone, and no apparent reaction occurred with HBr or thionyl chloride. The acetate, benzoate and tosylate were all oils.

When the vinylogous amide (IX, Z = $H_2$) was treated, at room temperature, with an ethanolic solution of perchloric acid a white crystalline salt was formed, from which the parent amide was released upon basification. The spectral characteristics of this perchlorate are entirely in accord with protonation of IX (Z = $H_2$) occurring at oxygen to yield XIII, in agreement with the behaviour of other vinylogous amides.[19] When XIII was warmed with a little perchloric acid a yellow solid was

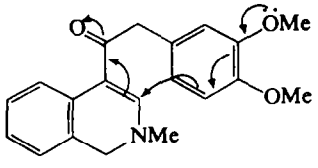

XIII



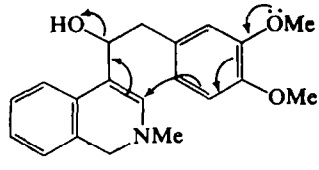

XIV

formed, from which the parent amide could not be recovered. The NMR spectrum of this yellow perchlorate (in $CF_3CO_2H$) was diagnostic for the fully aromatic structure XIV. Reduction of this material with sodium borohydride gave the saturated alcohol (XI); no evidence of a ring-closure could be found.

Various other attempts to ring-close IX (Z = $H_2$) all failed, probably because of the interaction of the nitrogen lone pair competing with the required intramolecular nucleophilic attack at $C_3$ (see XV). It was thought that the unsaturated alcohol (XVI)




XV

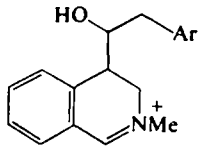



XVI

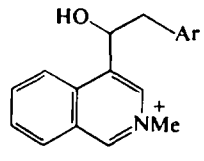
[18] See for example, Ref. 11, but see also the discussion in H. Reishagen, *Angew. Chem.* (Int. Ed). **4**, 710 (1965).

[19] G. H. Alt and A. J. Speziale, *J. Org. Chem.* **30**, 1407 (1965).

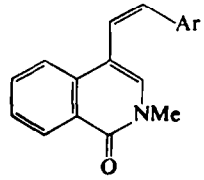
might provide a better substrate for the ring-closure. When the acetate of the saturated alcohol (XI) was dehydrogenated with iodine, two products were characterized. viz the 3,4-dihydroisoquinoline XVII and the fully aromatic structure (XVIII). Reduction of the latter with LAH followed by treatment of the intermediate 1,2-dihydroiso-




XVII




XVIII




XIX

quinoline with concentrated hydrochloric acid caused disproportionation to XI and XVIII. An attempt was made to ring-close the allylic alcohol (XII), in which the nitrogen lone pair electrons are not so available, but treatment with hydrochloric acid under mild conditions gave the dehydrated product (XIX).

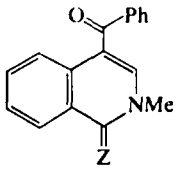
Since the acylation of a 1,2-dihydroisoquinoline constitutes a new method of preparation of 4-substituted isoquinolines, the scope of the reaction has been tested with a few other acid chlorides. The reaction between N-methyl-1,2-dihydroisoquinoline and acetyl chloride or crotonyl chloride gave complex mixtures from which it was not possible to isolate any pure material. With cinnamoyl chloride insufficient material could be isolated for study, although the NMR spectrum did

TABLE 1. THE ACYLATED ISOCARBOSTYRILS

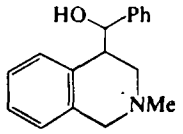
| R | Molecular formula | m.p.°m from ethanol | Yield* g | $\lambda_{max}$ | $\varepsilon_{max}$ | $\nu_{max}$ cm$^{-1}$ | Analysis Found C | H | N | Required C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Benzoyl | $C_{17}H_{13}NO_2$ | 134–5 | 1·2 | 226<br>296<br>307<br>320 | 21,340<br>11,190<br>11,650<br>8,421 | 1668, 1640<br>1625, 1605 | 77·8 | 5·2 | 5·2 | 77·55 | 5·0 | 5·3 |
| 3,4-Dimethoxy benzoyl | $C_{19}H_{17}NO_4$ | 179–80 | 0·92 | 222<br>283<br>324<br>340 | 31,420<br>15,560<br>18,110<br>13,210 | 1660, 1640,<br>1630, 1605 | 70·5 | 5·2 | 4·3 | 70·6 | 5·3 | 4·3 |
| Phenylacetyl | $C_{18}H_{15}NO_2$ | 208–10 | 1·25 | 233<br>285<br>305<br>317 | 29,510<br>29,210<br>25,300<br>16,260 | 1663, 1655<br>1625, 1605 | 77·8 | 5·6 | 5·1 | 78·0 | 5·45 | 5·05 |
| 3,4-Dimethoxyphenylacetyl | $C_{20}H_{19}NO_4$ | 167–8 | — | 298<br>323<br>335 | 16,800<br>14,300<br>10,100 | 1655, 1645<br>1620 | 71·05 | 5·7 | 4·2 | 71·2 | 5·7 | 4·15 |

* From 10 g isoquinoline methiodide.

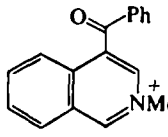
suggest that acylation had occurred as expected. Phenylacetyl, 3,4-dimethoxybenzoyl and benzoyl chlorides each reacted to give a $C_4$-acylated product, which was usually the isocarbostyril formed by oxidation during work up. The results are summarized in Table 1. In the case of benzoyl chloride fair yields of the vinylogous amide were obtained when N-methyl-1,2-dihydroisoquinoline was generated by the disproportionation of isoquinoline methiodide with alkali. Both XX ($Z = H_2$ and $Z = O$) were reduced to the saturated alcohol (XXI) with LAH. In this product too, the hydroxyl group was most unreactive. All attempts to convert (XX) or (XXI) to a




XX




XXI




XXII

derivative of the known[20] 4-benzylisoquinoline failed. The structures are, however, secure from the diagnostic NMR spectrum of the perchlorate (XXII) of XX ($Z = H_2$).

## EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken as nujol mulls unless otherwise stated and uv spectra were measured in EtOH solution.

*2-Methyl-1,2-dihydroisoquinoline* (I; R = Me). Dry, finely powdered isoquinoline methiodide (10 g) was added in small portions to a suspension of LAH (5 g) in anhydrous ether (500 ml) and the mixture was stirred for 12 hr. Excess LAH was decomposed with 30% aqueous potassium sodium tartrate under a protective atmosphere of $N_2$. The ethereal solution of I(R = Me) was decanted quickly and dried ($Na_2SO_4$) with the exclusion of atmospheric $O_2$.

*4-[3,4-Dimethoxyphenylacetyl]2-methyl-1,2-dihydroisoquinoline* (IX, $Z = H_2$). To the above ethereal solution of I(R = Me) was added $Et_3N$ (1 mole equiv) and then 3,4-dimethoxyphenylacetyl chloride (1 mole equiv) in dry benzene (100 ml) was added dropwise whilst a current of $N_2$ was passed through the apparatus. A gelatinous precipitate was immediately formed; the mixture was heated under reflux for 5 hours and water (50 ml) was then added to dissolve the solid matter. The organic layer was separated, washed with 2N HCl (2 × 25 ml), then with water (2 × 25 ml), dried ($MgSO_4$) and evaporated under reduced press to yield a brown gum. Trituration with EtOH gave IX($Z = H_2$) (1·6 g). After recrystallization from EtOH this had m.p. 116–118°. $\lambda_{max}$ m$\mu$ ($\varepsilon_{max}$) 230 (25,120), 287 (23,990) 345 (18,200). $\nu_{max}$ cm$^{-1}$ ($CHCl_3$) 1625, 1605, 1580. (Found: C, 73·9; H, 6·6; N, 4·5. $C_{20}H_{21}NO_3$ requires: C, 74·3; H, 6·55; N, 4·3%.)

Chromatography of the mother liquors over silica gel, and elution with chloroform petrol (60–80°) mixtures gave ethyl homoveratrate (2·4 g), 2-methylisocarbostyril (0·84 g) and *4-[3,4-dimethoxyphenylacetyl]2-methylisocarbostyril* (IX, Z = O) (0·5 g). See Table 1. The acetylated isocarbostryil (56 mg) was also produced when a solution of the vinylogous amide (100 mg) in acetone (25 ml) was shaken, at room temp, with $MnO_2$ (100 mg) for 5 hr.

*Other acylations of 2-methyl-1,2-dihydroisoquinoline.* These were carried out with benzoyl, 3,4-dimethoxybenzoyl and phenylacetyl chlorides as described above. In all cases only the acetylated isocarbostryil was isolated. The results are summarized in Table 1.

*4-Benzoyl-2-methyl-1,2-dihydroisoquinoline* (XX, $Z = H_2$). Isoquinoline methiodide (10 g) was dissolved in air-free water (100 ml), and a solution of NaOH (20 g) in water (30 ml) was added with

[20] J. Braun, O. Bayer and L. Cassel, *Ber. Dtsch. Chem. Ges.* **60**, 2602 (1927).

stirring. After 30 min the brown oil that had formed was extracted into ether (total 100 ml) and this organic liquid was dried ($Na_2SO_4$). Triethylamine (3 ml) and benzoyl chloride (2·1 ml) were added and the mixture was heated under reflux, with stirring for 5 hr. After the addition of water (50 ml), separation of the layers, drying and evaporation of the ether solution a brown gum remained which, on trituration with benzene afforded yellow plates of XX(Z = $H_2$). Recrystallization from benzene gave pale yellow plates, m.p. 67–69° (1·5 g). $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 288 (12,870) 295 (13,160) 323 (12,440). $\nu_{max}$ 1635, 1565. (Found: C, 84·2; H, 6·5; N, 4·5. $C_{17}H_{15}NO{\cdot}C_6H_6$ requires: C, 84·4; 6·5; N, 4·3%.)

When this compound was exposed to air, or chromatographed, or oxidized with active $MnO_2$, the acylated XX (Z = O) was produced.

4-[1-*Hydroxy*-2,3-(4-*dimethoxyphenyl*)*ethyl*]2-*methyl*-1,2,3,4-*tetrahydroisoquinoline* (XI). Sodium borohydride (50 mg) was added portionwise to a solution of IX (Z, = $H_2$) (100 mg) in EtOH (20 ml). The mixture was heated under reflux for 2 hr, the solvent was removed under reduced press and water (20 ml) was added. Extraction with ether (3 × 15 ml) followed by evaporation to dryness left a colourless meringue which could not be obtained crystalline. TLC on silica gel, with $CHCl_3$ containing 2% $Et_2NH$ as solvent, revealed two spots ($R_f$ 0·87 and 0·83), thought to be due to the two enantiomorphs of (XI). The methiodide of XI was obtained from EtOH–$Et_2O$, m.p. 80–92°. (Found: C, 53·85; H, 6·05; N, 2·8. $C_{21}H_{28}INO_2$ requires: C, 53·7; H, 6·0; N, 3·0%.)

Acetylation of XI gave an oil, the methiodide of which crystallized from EtOH as colourless needles, m.p. 224–226°. (Found: C, 54·3; H, 5·7; H, 2·5. $C_{23}H_{30}INO_4$ requires: C, 54·0; H, 5·9; N, 2·7%.)

The same saturated alcohol was obtained by reduction of IX (Z = $H_2$ or Z = O) with LAH under the usual conditions.

*Dehydrogenation of* 4-[1-*acetoxy*-2-(3,4-*dimethoxyphenyl*)*ethyl*]2-*methyl*-1,2,3,4-*tetrahydroisoquinoline*. The O-acetyl derivative of (XI) (700 mg) in EtOH (20 ml) containing anhydrous AcONa (1·5 g) was heated on a waterbath whilst a solution of $I_2$ (2 g) in EtOH (20 ml) was added slowly. After 3 hr heating, the straw-coloured solution was evaporated to low bulk and water (10 ml) added. $SO_2$ was bubbled through the solution until the $I_2$ colour was discharged. On standing yellow crystals of XVIII were deposited (150 gm). Recrystallization from EtOH gave m.p. 175–176°. $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 235 (24,500), 280 (7,000) $\nu_{max}$ cm$^{-1}$ 3400, 1640, 1620. (Found: C, 53·0; H, 5·1; N, 3·0. $C_{20}H_{22}INO_2$ requires: C, 53·2; H, 4·9; N, 3·1%.)

The original mother liquors were extracted with $CHCl_3$, which was then evaporated to leave a brown resin, partially soluble in hot water. KCN was added to the aqueous solution when the pseudocyanide of 4-[1-*hydroxy*-2(3,4-*dimethoxyphenyl*)*ethyl*]2-*methyl*-3,4-*dihydroisoquinoline* (XI) separated. Recrystallization from benzene–petrol (b.p. 60–80° 1:1) gave colourless needles m.p. 114–115°. (Found: C, 71·55; H, 6·7; N, 7·7. $C_{21}H_{24}N_2O_2$ requires: C, 71·6; H, 6·9; N, 8·0%.) The corresponding 3,4-dihydroisoquinolinium iodide crystallized as yellow needles from EtOH m.p. 184–186°. $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 220 (32,050), 286 (15,000) $\nu_{max}$ 1670 cm$^{-1}$. (Found: C, 53·25; H, 5·1; N, 3·0. $C_{20}H_{24}INO_2$ requires: C, 53·0; H, 5·3; N, 3·1%.)

4-[3,4-*Dimethoxyphenylacetyl*]2-*methylisoquinolinium perchlorate* (XIV); The amide IX (Z = $H_2$; 0·5 g) in EtOH (10 ml) was treated with 60% aqueous perchloric acid (1 ml). After standing overnight, colourless crystals had separated (0·42 g). Recrystallization from EtOH gave XIII as colourless prisms, m.p. 178–180°. $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 237 (34,670) 280, (12,300), 240 (11,750); $\nu_{max}$ cm$^{-1}$ 3300, 1662, 1610. (Found: C, 56·3; H, 5·5; N, 3·2. $C_{20}H_{21}NO_3{\cdot}HClO_4$ requires: C, 56·7; H, 5·2; N, 3·3%.)

When a quantity of this perchlorate was warmed in EtOH containing a little perchloric acid, yellow needles of XIV were deposited (82% conversion). Recrystallization from $CHCl_3$ gave yellow needles, m.p. 188–189°. $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 232 (26,300), 281 (13,700), 333 (12,250); $\nu_{max}$ cm$^{-1}$ 17,00 1645, 1615. (Found: C, 56·7; H, 5·0; N, 3·6. $C_{20}H_{20}NO_3{\cdot}HClO_4$ requires: C, 56·9; H, 4·8; N, 3·3%.)

4-*Benzoyl*-2-*methylisoquinolinium perchlorate* (XXII). The amide XX (Z = $H_2$; 100 mg) in EtOH (10 ml) was warmed with 60% aqueous perchloric acid (1 ml). When cooled, a crystalline deposit (85 mg) of XXII formed. Recrystallization from EtOH gave yellow needles, m.p. 216–218°; $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 221 (41,320), 323 (6,071); $\nu_{max}$ cm$^{-1}$ 1665, 1645, 1635. (Found: C, 58·7; H, 4·3; N, 3·7. $C_{17}H_{14}NO{\cdot}HClO_4$ requires: C, 58·7; H, 4·1; N, 4·0%.)

4-[1-*Hydroxy*-2-(3,4-*dimethoxyphenyl*)*ethyl*]2-*methylisocarbostyril* (XII). Sodium borohydride

(150 mg) was added in small portions to a suspension of IX (Z = O; 150 mg) in MeOH (20 ml). After heating the mixture under reflux for 2 hr, the solvent was removed and water (20 ml) added. Extraction with benzene (3 × 15 ml) afforded a gum which, upon trituration with ether, gave colourless prisms (120 mg). Recrystallization from EtOH gave colourless prisms of XII, m.p. 150–151°; $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 230 (25,900), 285 (9,770), 330 (4,250); $\nu_{max}$ cm$^{-1}$ 3375, 1650, 1625. (Found: C, 70·7; H, 6·3; N, 4·0. $C_{20}H_{21}NO_4$ requires: C, 70·8; H, 6·2; N, 4·1%.)

Treatment of XX (Z = O) with $NaBH_4$ in MeOH at room temp yielded a product corresponding to XII m.p. 171–172° as small white needles. (Found: C, 76·5; H, 5·2; N, 5·6; $C_{17}H_{15}NO_3$ requires: C, 77·0; H, 5·7; N, 5·13%.) Reduction of either XX (Z = $H_2$) or (Z = O) with LAH under standard conditions gave XXI. The methiodide was obtained from EtOH as small prisms m.p. 123–125°. (Found: C, 55·4; H, 6·2; N, 3·4; I, 32·55. $C_{18}H_{22}INO$ requires: C, 54·9; H, 5·8; N, 3·5; I, 32·1%.)

4-[3,4-*Dimethoxystyril*]2-*methylisocarbostyril* (XIX). A solution of XII (50 mg) in benzene was saturated with HCl during 15 min. Removal of the solvent under reduced press gave a crystalline residue, recrystallization of which from AcOEt yielded XIX (36 mg) as stout colourless prisms, m.p. 132–134°; $\lambda_{max}$ m$\mu$($\varepsilon_{max}$) 278 (16,000), 333 (21,750); $\nu_{max}$ cm$^{-1}$ 1640, 1635, 1615. (Found: C, 74·7; H, 6·1; N, 4·8; OMe, 19·2. $C_{18}H_{13}NO(OMe)_2$ requires; C, 74·7; H, 6·0; N, 4·40 OMe, 19·35%.)