Studies on the Syntheses of Heterocyclic Compounds. Part 681.† A Novel Alkylation in the 4-Position of Isoquinoline Derivatives

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Alkylations of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (1) with 2-methylcyclohex-2-enone (4) and with phenethyl bromide (19) in the presence of sodium hydride and dimethyl sulphoxide gave the 4-(2-methyl-3-oxocyclohexyl) (6) and 4-phenethyl (20) derivatives, respectively, of 6,7-dimethoxy-1-methylisoquinoline. The reaction of compound (1) with 1,4-naphthoquinone (7) under the same conditions afforded 7-methoxy-1-methyl-6-methylsulphinylmethylisoquinoline (12) as a major product and several minor products. Compound (12) was converted into 7-methoxy-1,6-dimethylisoquinoline (13), synthesised alternatively from 4-methoxy-3-methylbenzaldehyde (14).

REPORTED procedures for alkylation and acylation at the 4-position of isoquinoline derivatives include modifications of the Pomeranz–Fritsch reaction,[1] reactions of acyl and alkyl halides with 1,2-dihydroisoquinoline derivatives,[2-4] reactions of 4-lithioisoquinoline with carbon dioxide[5] and aldehydes,[3] and reactions of 4,7-diacetoxy-1,2,3,4-tetrahydroisoquinolines with active methylene compounds.[6] However, since the reactions of 1,2-dihydroisoquinoline derivatives with alkyl halides did not proceed in high yield, we have explored alternative routes to 4-substituted isoquinolines. Here we report a new method of alkylation at the 4-position of a 3,4-dihydroisoquinoline through an enamine intermediate.

At first, we studied enamine formation from 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline[7] (1) under basic conditions, to determine which enamine, (2) or (3), would be formed as an intermediate. A mixture of the 3,4-dihydroisoquinoline (1) and 2-methylcyclohex-2-enone[8] (4) (to trap the enamine) was kept at room temperature for 30 min in sodium hydride and dimethyl sulphoxide. 6,7-Dimethoxy-1-methyl-4-(2-methyl-3-oxocyclohexyl)isoquinoline (6) was obtained in 25.7% yield. The i.r. spectrum showed saturated six-membered ring ketone absorption at 1 700 cm^{-1} ($CHCl_3$), and the n.m.r. spectrum ($CDCl_3$) exhibited signals for an aliphatic methyl group at δ 0.88 (d, J 6 Hz) and for the aromatic

† Part 680, T. Kametani, T. Uryu, and K. Fukumoto, preceding paper.

[1] J. M. Bobbitt, K. L. Khanna, and J. M. Kieley, *Chem. and Ind.*, 1964, 1950; J.M. Bobbitt, J. M. Kieley, K. L. Khanna, and R. Ebermann, *J. Org. Chem.*, 1965, **30**, 2247; J. M. Bobbitt, D. P. Winter, and J. M. Kieley, *ibid.*, p. 2459.

[2] S. F. Dyke, M. Sainsbury, D. W. Brown, M. N. Palfreyman, and E. P. Tiley, *Tetrahedron*, 1968, **24**, 6703.

[3] M. Sainsbury, D. W. Brown, S. F. Dyke, R. D. J. Clipperton, and W. R. Tonkyn, *Tetrahedron*, 1970, **26**, 2239.

[4] T. K. Chen and C. K. Bradsher, *Tetrahedron*, 1973, **29**, 1951.

[5] H. Gilman and T. S. Soddy *J. Org. Chem.* 1957, **22**, 565.

[6] O. Hoshino, Y. Yamanashi, T. Toshioka, and B. Umezawa, *Chem. and Pharm. Bull. (Japan)*, 1971, **19**. 2166.

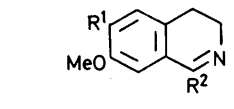
[7] E. Späth and N. Polgar, *Monatsh.*, 1929, **51**, 197.

[8] E. W. Warnhoff, D. G. Martin, and W. S. Johnson, *Org. Synth.*, Coll. Vol. 4. 1963, p. 162.

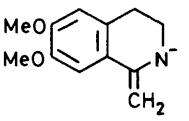
C-3 proton at δ 8.26 (s). These data suggested that the cyclohexanone was attached to C-4 [$\lambda_{max.}$ (MeOH) 314 and 326 nm], and this fact was rationalised in terms of formation of the enamine (3) and Michael addition of the enamine to 2-methylcyclohex-2-enone to form compound (5), followed by dehydrogenation. Having thus established that the 3,4-dihydro-1-methylisoquinoline (1) formed the enamine (3) under basic conditions, we examined the behaviour of the latter in cycloaddition reactions.

A mixture of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (1) and 1,4-naphthoquinone (7) was heated at 70 °C for 1 h. No tetracyclic compound product was observed, but the reaction afforded five compounds (8)—(12) in 2.9, 7.4, 7.47, 2.3, and 16.8% yield, respectively. Compound (8) contained sulphur but no nitrogen; the i.r. spectrum showed a carbonyl band (1 660 cm^{-1}) and n.m.r. spectrum ($CDCl_3$) revealed the presence of an *S*-methyl group [δ 2.36 (s)], four aromatic protons of an α-naphthoquinone (δ 7.5—8.13), and an olefinic proton [δ 6.53 (s)]. Compound (9) showed a naphthoquinone carbonyl band at 1 660 cm^{-1} ($CHCl_3$) and the n.m.r. spectrum ($CDCl_3$) showed the presence of a methyl group [δ 2.9 (s)], four aromatic protons in a 1,4-naphthoquinone (δ 7.7—8.3), and the C-3 proton of an isoquinoline ring [δ 8.03 (s)]. The product (10) was identified as 6,7-dimethoxy-1-methylisoquinoline from spectral data and direct comparison with an authentic specimen.[9] Compound (11), which contained a naphthoquinone system [$\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1}, δ ($CDCl_3$) 7.7—8.3 (4 H, m)], exhibited n.m.r. signals for two methyl groups at δ 2.7 as a singlet (6 H), and two isoquinoline C-3 protons at δ 8.02 as a singlet. The last product exhibited n.m.r. signals for a methylsulphinyl group (δ 2.5), methylene protons located between a sulphinyl group and an aromatic ring (δ 4.21), protons C-3 and C-4 aromatic (δ 8.27 and 7.40; each d, *J* 6 Hz), a *C*-methyl and an *O*-methyl group, and two isolated aromatic protons. Treatment of this product with zinc in acetic acid afforded, in 96% yield, a desulphurisation product, δ 2.36, 2.87, and 3.95 (each s, Me) (no CH_2 signal). This evidence did not distinguish between 7-methoxy-1-methyl-6-methylsulphinylmethyl- (12) and 6-methoxy-1-methyl-7-methylsulphinylmethyl-isoquinoline as the structure of the original product. We therefore carried out an alternative synthesis of compound (13), the desulphurisation product of (2).

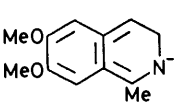
4-Methoxy-3-methylbenzaldehyde[10] (14) was condensed with nitromethane in boiling acetic acid in the presence of ammonium acetate to give the nitrostyrene (15), which was reduced with lithium aluminium hydride to afford 4-methoxy-3-methylphenethylamine (16).[11] The amine was treated with acetic anhydride–pyridine to give the acetamide (17), which was cyclized in the presence of phosphoryl chloride in acetonitrile to afford the 3,4-dihydro-7-methoxy-1,6-dimethylisoquinoline (18) [δ ($CDCl_3$) 2.22 and 2.38 (each 3 H, s, Me)]. This 3,4-dihydroisoquinoline was dehydrogenated with sodium hydride in dimethyl sulphoxide at 70 °C to give 7-methoxy-1,6-dimethylisoquinoline (13), which was identical with the foregoing desulphurisation product. Thus, the fifth product was identified as 7-methoxy-1-methyl-6-methylsulphinylmethylisoquinoline (12).



(1) R^1 = OMe, R^2 = Me
(18) R^1 = R^2 = Me
(22) R^1 = OMe, R^2 = H



(2)



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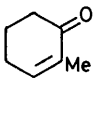
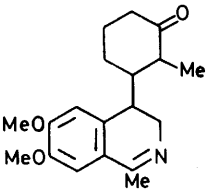


(4)



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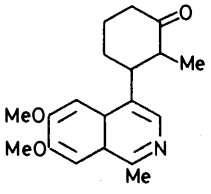
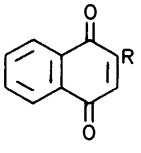
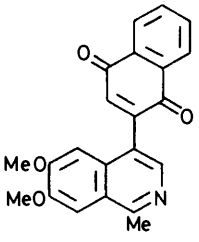


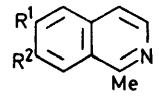
(6)



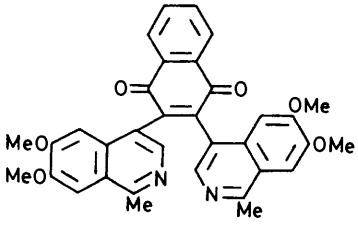
(7) R = H
(8) R = SMe



(9)



(10) R^1 = R^2 = OMe
(12) R^1 = MeS(O)CH_2, R^2 = OMe
(13) R^1 = Me, R^2 = OMe



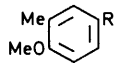
(11)

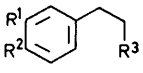
[9] Von H. Bruderer and A. Brossi, *Helv. Chim. Acta*, 1965, **48**, 1945.

[10] R. A. Barnes and N. N. Gerber, *J. Org. Chem.*, 1961, **20**, 4540; N. P. Buu-Hoï, N. D. Xuong, M. Sy, G. Lejeune, and N. B. Tien. *Bull. Soc. chim. France*, 1955, 1694.

[11] S. N. Kulkarni, S. B. Patil, P. V. Panchangam, and K. S. Nargund, *Indian J. Chem.*, 1967, **5**, 471.

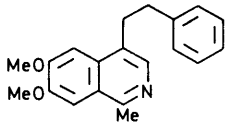
Alkylation of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (1) was then attempted with phenethyl bromide (19), at 60 °C for 1 h, and the expected 4-phenethylisoquinoline (20) was obtained in 20.5% yield [δ ($CDCl_3$) 2.98—3.26 (2 CH_2), 8.06 (H-3), and 2.83, 3.91, and 3.96 (3 Me)]. 3,4-Dihydro-6,7-dimethoxyisoquinoline [12] (22) was then treated with 3,4-methylenedioxyphenethyl bromide [13] (21) under the same conditions, but two unexpected compounds, (24) and (10), were obtained, in 17 and 12.7% yield, respectively. Compound (24), *m/e* 226 (M^+), showed n.m.r. signals for a methylsulphinyl group at δ 2.55 (singlet) and three methylene groups at 1.6—3.0. The product (10) showed signals for a *C*-methyl group at δ 2.88 (singlet) and aromatic C-3 and C-4 protons at 8.22 and 7.32 (doublets, *J* 6 Hz) in addition to two isolated aromatic protons. The product was in fact identical with authentic 6,7-dimethoxy-1-methylisoquinoline (10).[9]



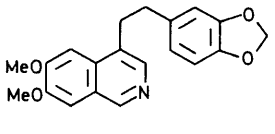


(14) R = CHO
(15) R = CH:CH·NO_2
(16) R = $[CH_2]_2$·NH_2
(17) R = $[CH_2]_2$·NHAc

(19) R^1 = R^2 = H, R^3 = Br
(21) R^1 R^2 = O·CH_2·O, R^3 = Br
(24) R^1 R^2 = O·CH_2·O, R^3 = CH_2·S(O)Me



(20)



(23)

Thus the expected 4-phenethylisoquinoline (23) was not formed from a 3,4-dihydroisoquinoline (22) having no methyl group at C-1.

EXPERIMENTAL

M.p.s were measured with a Yanagimoto micro apparatus (MP-S2). I.r. spectra were measured with a Hitachi 215 grating spectrophotometer, n.m.r. spectra with JEOL PMX-60 and JEOL JNM-PS-100 spectrometers (tetramethylsilane as an internal standard), mass spectra with a Hitachi RMU-7 spectrometer, and u.v. spectra with a Hitachi 124 spectrometer.

6,7-Dimethoxy-1-methyl-4-(2-methyl-3-oxocyclohexyl)isoquinoline (6).—Sodium hydride (50% in oil; 1.0 g) was added to dimethyl sulphoxide (20 ml), and the mixture was stirred for 1 h at 70 °C, then cooled in ice while a solution of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (1) (400 mg) in dimethyl sulphoxide (5 ml) was added. The resulting mixture was stirred for 1 h at 60 °C, then a solution of 2-methylcyclohex-2-enone [8] (4) (220 mg) in dimethyl sulphoxide (5 ml) was added. The mixture was stirred for a further 30 min at room temperature, then water was added and the mixture was extracted with ether. The ethereal solution was extracted with 10% hydrochloric acid, and the aqueous acidic layer was washed with ether and basified with 10% ammonium hydroxide. The aqueous layer was again extracted with ether and the ethereal layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to leave an oil, which was subjected to column chromatography on silica gel (5 g). Elution with chloroform gave the *4-cyclohexylisoquinoline* (6) (157 mg, 25.7%) as needles (from methanol), m.p. 183—184° (Found: C, 72.4; H, 7.45; N, 4.35. $C_{19}H_{23}NO_3$ requires C, 72.85; H, 7.35; N, 4.45%), $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1} (C=O), δ ($CDCl_3$) 0.88 (3 H, d, *J* 6 Hz, CH*Me*), 2.88 (3 H, s, 1-Me), 4.03 (6 H, s, 2 × OMe), 7.17 (1 H, s, ArH), 7.25 (1 H, s, ArH), and 8.26 (1 H, s, 3-H), *m/e* 313 (M^+).

Reaction of 3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline (1) *with 1,4-Naphthoquinone* (17).—A solution of sodium hydride (50% in oil; 2.4 g) in dimethyl sulphoxide (30 ml) was stirred for 1 h at 70 °C, then cooled in ice while a solution of the 3,4-dihydroisoquinoline (1) (1 g) in dimethyl sulphoxide (10 ml) was added. The mixture was stirred for 1 h at 70 °C, then a solution of 1,4-naphthoquinone (7) (790 mg) in dimethyl sulphoxide (10 ml) was added. The resulting mixture was stirred for 1 h at 70 °C, then water was added and the mixture was extracted with chloroform. The organic layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to leave a gum which was subjected to column chromatography on silica gel (60 g). Elution with benzene afforded *2-methylthio-1,4-naphthoquinone* (8) (30 mg, 2.9%) as yellowish needles (from ethanol), m.p. 165—166° (Found: C, 64.55; H, 4.0. $C_{11}H_8O_2S$ requires C, 64.7; H, 3.95%), $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1} (C=O), δ ($CDCl_3$) 2.36 (3 H, s, 2-SMe), 6.53 (1 H, s, 3-H), and 7.5—8.13 (4 H, m, ArH), *m/e* 204 (M^+). Elution with benzene–methanol (99 : 1 v/v) then gave *6,7-dimethoxy-1-methyl-4-(1,4-naphthoquinon-2-yl)isoquinoline* (9) (130 mg, 7.4%) as reddish needles (from methanol), m.p. 218—220° (Found: C, 72.85; H, 4.7; N, 3.8. $C_{22}H_{17}O_4$,0.25H_2O requires C, 72.6; H, 4.85; N, 3.85%), $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1} (C=O), δ ($CDCl_3$) 2.9 (3 H, s, 1-Me), 3.83 (3 H, s, OMe), 4.0 (3 H, s, OMe), 6.76 (1 H, s, ArH), 7.10 (1 H, s, ArH), 7.23 (1 H, s, ArH), 7.7—8.3 (4 H, m, ArH), and 8.03 (1 H, s, 3-H), *m/e* 359 (M^+), followed by 6,7-dimethoxy-1-methylisoquinoline (10) (74 mg, 7.47%), needles (from n-hexane), m.p. 110—111° (lit.,[9] 110—111°), $\lambda_{max.}$ (MeOH) 312 and 325 nm, δ ($CDCl_3$) 2.89 (3 H, s, 1-Me), 4.0 (6 H, s, 2 × OMe), 6.9—7.5 (3 H, m, ArH), and 8.2 (1 H, d, *J* 6 Hz, 3-H), *m/e* 203 (M^+). Elution with benzene–methanol (49 : 1 v/v) gave *2,3-bis-(6,7-dimethoxy-1-methylisoquinolin-4-yl)-1,4-naphthoquinone* (11) (154 mg, 2.3%) as yellowish needles (from benzene), m.p. >300° (Found: C, 70.45; H, 5.0. $C_{34}H_{28}N_2O_6$,H_2O requires C, 70.55; H, 5.25%), $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1} (C=O), δ ($CDCl_3$) 2.7 (6 H, s, 2 × Me), 3.93 (6 H, s, 2 × OMe), 4.0 (6 H, s, 2 × OMe), 6.83 (2 H, s, ArH), 7.20 (2 H, s, ArH), 7.7—8.3 (4 H, m, ArH), and 8.02 (2 H, s, 3-H), *m/e* 560 (M^+). Elution with benzene–methanol (97 : 3 v/v) afforded *7-methoxy-1-methyl-6-methylsulphinylmethylisoquinoline* (12) (204 mg, 16.8%) as needles (from n-hexane), m.p. 116—117° (Found: C, 62.5; H, 6.05; N, 5.65. $C_{13}H_{15}NO_2S$ requires C, 62.6; H, 6.05; N, 5.6%), δ ($CDCl_3$) 2.5 (3 H, s, SOMe), 2.9 (3 H, s, 1-Me), 4.0 (3 H, s, OMe), 4.21 (2 H, s, CH_2·SO), 7.28 (1 H, s, ArH), 7.70 (1 H, s, ArH), 7.40 (1 H, d, *J* 6 Hz, 4-H), and 8.27 (1 H, d, *J* 6 Hz, 3-H), *m/e* 249 (M^+).

Reaction of the 6-Methylsulphinylmethylisoquinoline (12)

[12] W. M. Whaley and M. Meadow, *J. Chem. Soc.*, 1953, 1067.
[13] S. Sugasawa and Y. Suzuta, *J. Pharm. Soc. Japan*, 1951, **71**, 1159.

with Zinc in Acetic Acid.—Activated zinc dust (450 mg) and acetic acid (20 ml) were added to a solution of the isoquinoline (12) (170 mg) in ethanol (10 ml). The mixture was stirred for 2 h at room temperature and refluxed for 2 h. After removal of zinc, the solvent was distilled off *in vacuo* and the residue was basified with 10% ammonium hydroxide and extracted with chloroform. The organic layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to give 7-*methoxy*-1,6-*dimethylisoquinoline* (13) (120 mg, 96%), which was purified by sublimation to afford needles, m.p. 84—85° (Found: C, 75.85; H, 6.95; N, 7.25. $C_{12}H_{13}NO,0.17H_2O$ requires C, 75.75; H, 7.05; N, 7.35%), δ ($CDCl_3$) 2.36 (3 H, s, 6-Me), 2.87 (3 H, s, 1-Me), 3.95 (3 H, s, OMe), 7.16—7.53 (3 H, m, ArH), and 8.21 (1 H, d, *J* 6 Hz, 3-H), *m/e* 187 (M^+); the hydrochloride formed needles (from methanol–ether), m.p. 250° (decomp.).

4-*Methoxy*-3-*methyl*-β-*nitrostyrene* (15).—A mixture of 4-methoxy-3-methylbenzaldehyde [10] (14) (5 g), nitromethane (4 g), ammonium acetate (3.9 g), and acetic acid (30 ml) was refluxed for 2 h. The mixture was then poured into water to give a yellowish solid, which was recrystallised from ethanol to give the *nitrostyrene* (15) (2.5 g, 39%) as yellowish needles, m.p. 76—77° (Found: C, 62.15; H, 5.65; N, 7.5. $C_{10}H_{11}NO_3$ requires C, 62.15; H, 5.75; N, 7.25%), $\nu_{max.}$ 1 620 (C=C) and 1 330 cm^{-1} (NO_2), δ ($CDCl_3$) 2.22 (3 H, s, Me), 3.89 (3 H, s, OMe), 6.76—7.42 (3 H, m, ArH), 7.45 (1 H, d, *J* 14 Hz, olefinic), 7.95 (1 H, d, *J* 14 Hz, olefinic).

4-*Methoxy*-3-*methylphenethylamine* (16).—A solution of the nitrostyrene (15) (6 g) in tetrahydrofuran (50 ml) was added to a suspension of lithium aluminium hydride (4 g) in tetrahydrofuran. The mixture was then refluxed for 1 h, 15% sodium hydroxide was added, and the inorganic precipitate was filtered off. Evaporation afforded a residue which was extracted with benzene. The organic layer was washed with saturated sodium chloride solution, dried (K_2CO_3), and evaporated to leave a yellowish oil, which was distilled to give 4-methoxy-3-methylphenethylamine (16) (3 g, 59%) as an oil, b.p. 95—100° at 4 mmHg (lit.,[11] 245—250° at 710 mmHg).

N-(4-*Methoxy*-3-*methylphenethyl*)*acetamide* (17).—A solution of the amine (16) and acetic anhydride (2.5 g) in pyridine (20 ml) was stirred for 2 h at room temperature. Then water (10 ml) was added and the mixture was extracted with chloroform. The organic layer was washed with 10% hydrochloric acid and saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to give the *amide* (17) (3.5 g, 92%) as needles, m.p. 58—59° (from n-hexane) (Found: C, 69.05; H, 8.0; N, 6.4. $C_{12}H_{17}NO_2,0.1H_2O$ requires C, 68.95; H, 8.3; N, 6.7%), $\nu_{max.}$ ($CHCl_3$) 1 660 cm^{-1} (C=O), δ ($CDCl_3$) 1.90 (3 H, s, Ac), 2.19 (3 H, s, 3-Me), 2.71 (2 H, t, *J* 7.5 Hz, $PhCH_2{\cdot}CH_2N$), 3.41 (2 H, t, *J* 7.5 Hz, $PhCH_2{\cdot}CH_2{\cdot}N$), 3.77 (3 H, s, OMe), and 6.63—7.1 (3 H, m, ArH).

3,4-*Dihydro*-7-*methoxy*-1,6-*dimethylisoquinoline* (18).—A mixture of the amide (17) (3.4 g), phosphoryl chloride (3.0 g), and acetonitrile (30 ml) was refluxed for 6 h, then evaporated. The residue was washed with ether, basified with 10% ammonium hydroxide solution, and extracted with chloroform. The organic layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to leave an oil, which was purified by column chromatography on silica gel (60 g) with chloroform to give the 3,4-dihydroisoquinoline (18) (1.3 g, 42%) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 620 cm^{-1} (C=N), δ ($CDCl_3$) 2.22 (3 H, s, 1-Me), 2.38 (3 H, s, 6-Me), 2.36—2.8 (2 H, m, $PhCH_2{\cdot}CH_2{\cdot}N$), 3.41—3.84 (2 H, m, $PhCH_2{\cdot}CH_2{\cdot}N$), 3.84 (3 H, s, OMe), and 6.86br (2 H, s, ArH), *m/e* 189 (M^+). The *picrate* formed yellowish needles, m.p. 235—236° (from ethanol) (Found: C, 51.7; H, 4.35. $C_{18}H_{18}N_4O_7,H_2O$ requires C, 51.4; H, 4.8%).

7-*Methoxy*-1,6-*dimethylisoquinoline* (13).—A mixture of sodium hydride (50% in oil; 1.25 g) and dimethyl sulphoxide (20 ml) was stirred for 1 h at 70 °C. A solution of the 3,4-dihydroisoquinoline (18) (500 mg) in dimethyl sulphoxide (5 ml) was then added and the mixture was stirred for 1 h at 70 °C. After addition of ice–water, the mixture was extracted with 10% hydrochloric acid. The aqueous layer was basified with 10% ammonium hydroxide and extracted with ether. The organic layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to give the isoquinoline (13) (300 mg, 60.8%) which was purified by sublimation to give needles, m.p. 84—85°. The hydrochloride formed needles (from methanol–ether), m.p. 250° (decomp.), identical with the sample prepared previously [i.r. spectrum (KBr)].

6,7-*Dimethoxy*-1-*methyl*-4-*phenethylisoquinoline* (20).—A mixture of sodium hydride (50% in oil; 1.44 g) and dimethyl sulphoxide (20 ml) was stirred for 1 h at 70 °C. A solution of the 3,4-dihydro-1-methylisoquinoline (1) (615 mg) in dimethyl sulphoxide (5 ml) was then added and the mixture was stirred for 1 h at 65 °C. A solution of phenethyl bromide (19) (555 mg) in dimethyl sulphoxide (5 ml) was then added and the mixture was stirred for 1 h at 70 °C, then decomposed with water and extracted with ether. The ethereal layer was extracted with 10% hydrochloric acid. The aqueous layer was basified with 10% ammonium hydroxide and extracted with ether. The organic layer was washed with saturated sodium chloride solution, dried (K_2CO_3), and evaporated to leave an oil, which was chromatographed on silica gel (30 g) with chloroform to give the 4-phenethylisoquinoline (20) (189 mg, 20.5%) as an oil, $\lambda_{max.}$ (MeOH) 315 and 327 nm, δ ($CDCl_3$) 2.83 (3 H, s, 1-Me), 2.98—3.26 (4 H, m, $CH_2{\cdot}CH_2$), 3.91 (3 H, s, OMe), 3.96 (3 H, s, OMe), 7.0—7.33 (7 H, m, ArH), and 8.06 (1 H, s, 3-H), *m/e* 307 (M^+). The *picrate* had m.p. 210—211° (decomp.) (from ethanol) (Found: C, 57.95; H, 4.65; N, 10.05. $C_{26}H_{24}N_4O_9$ requires C, 58.2; H, 4.5; N, 10.45%).

Reaction of 3,4-*Dihydro*-6,7-*dimethoxyisoquinoline* (22) *with* 3,4-*Methylenedioxyphenethyl Bromide* (21).—Sodium hydride (50% in oil; 1.4 g) in dimethyl sulphoxide (30 ml) was stirred for 1 h at 70 °C, then a solution of the 3,4-dihydroisoquinoline (22) (573 mg) in dimethyl sulphoxide (5 ml) was added. The mixture was stirred for 30 min at 60 °C and a solution of the phenethyl bromide (21) in dimethyl sulphoxide (5 ml) was added. Stirring was continued for 3 h at 70 °C, then ice–water was added, and the mixture was extracted with ether. The ethereal layer was extracted with 10% hydrochloric acid and the extract was washed with ether. The aqueous layer was basified with 10% ammonium hydroxide solution and extracted with ether. The organic layer was washed with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to leave an oil, which was subjected to column chromatography on silica gel (30 g). Elution with benzene–ethyl acetate (95 : 5 v/v) afforded the 1-methylisoquinoline (10) (73 mg, 12.3%) as needles (from n-hexane), m.p. 110—111° (lit.,[9] 110—111°), identical with an authentic specimen [9] [i.r. spectrum ($CHCl_3$)]. Elution with benzene–ethyl

acetate (4 : 1 v/v) gave methyl 3-(3,4-methylenedioxyphenyl)propyl sulphoxide (24) (123 mg, 17%) as an oil, δ ($CDCl_3$) 2.55 (3 H, s, SOMe), 1.6—3.0 (6 H, m, CH_2·CH_2·CH_2), 5.39 (2 H, s, O·CH_2·O), and 6.7br (3 H, s, ArH), *m/e* 226 (M^+).

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