STUDIES IN THE ISOQUINOLINE SERIES

Part III. Synthesis of Some 5 : 6—and 5 : 8—Dimethoxyisoquinolines

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Although papaverine is a valuable antispasmodic drug used in current clinical practice, the search for a better spasmolytic drug has never abated. Eupapaverine[1] and Neupaverine[2] are products of this effort. Several 1-dialkoxyphenyl and 1-dialkoxyphenethyl isoquinolines have been shown to have considerable spasmolytic activity.[3] It has been claimed that 3-methylisoquinolines have lowered toxicity than the 3-unsubstituted analogues. The work reported in this paper forms part of a programme of work on spasmolytic drugs in progress in this laboratory.[4]

β-(2 : 5-Dimethoxyphenyl) ethyl amine[5] was prepared by the lithium aluminium hydride reduction of 2 : 5-dimethoxy-ω-nitrostyrene. Its formyl, acetyl, benzoyl and phenylacetyl derivatives were smoothly cyclised by phosphorus oxychloride to 3 : 4-dihydro-5 : 8-dimethoxy-, 3 : 4-dihydro-5 : 8-dimethoxy-1-methyl-, 3 : 4-dihydro-5 : 8-dimethoxy-1-phenyl-, and 3 : 4-dihydro-5 : 8-dimethoxy-1-benzylisoquinolines respectively.

Similarly, from β-(2 : 5-dimethoxyphenyl) isopropyl amine,[6] prepared by the lithium aluminium hydride reduction of 2 : 5-dimethoxy-β-methyl-ω-nitrostyrene, the corresponding 3 : 4-dihydro-3-methylisoquinolines were prepared.

β-(2 : 3-Dimethoxyphenyl) ethyl amine[7] was prepared by the reduction of 2 : 3-dimethoxy-ω-nitrostyrene. β-2 : 3-dimethoxyphenylisopropyl amine was prepared by the Hofmann degradation of β-2 : 3-dimethoxyphenyl-α-methylpropionamide. The formyl, acetyl, benzoyl and phenylacetyl derivatives of these amines were cyclised to the corresponding 3 : 4-dihydro- and 3 : 4-dihydro-3-methylisoquinolines.

Reduction of 2 : 4-dimethoxy-ω-nitrostyrene and of 2 : 4-dimethoxy-β-methyl-ω-nitrostyrene with lithium aluminium hydride led to 2 : 4-dimethoxyphenylethyl amine and 2 : 4-dimethoxyphenylisopropyl amine respectively. The amides derived from either of these amines could not be made to yield the corresponding 3 : 4-dihydro-5 : 7-dimethoxyisoquinolines under any condition. The cumulative inductive deactivation of the position of cyclisation by both the methoxyl groups which are meta to this position should be res-

ponsible for this failure. A single methoxyl group meta to the point of cyclisation has been shown to inhibit ring closure.[8]

All the 3-methyl-3 : 4-dihydroisoquinolines underwent dehydrogenation with remarkable facility by heating in decalin solution with palladised charcoal (5% Pd). Dehydrogenation of 3 : 4-dihydroisoquinolines with a substituent at the 1-position, but not having a substituent at the 3-position, was more difficult, requiring a higher temperature and longer duration. Dehydrogenation of 3 : 4-dihydroisoquinolines without a substituent either at the 3- or 1-positions could not be effected using palladised charcoal, but was achieved only with palladium black as catalyst.

Experimental Procedure

ω-Nitrostyrenes.—These were prepared by the following procedure which is illustrated in the case of 2 : 5-dimethoxy-β-methyl nitrostyrene.

A mixture of 2 : 5-dimethoxybenzaldehyde (10 g.), nitroethane (10 ml.), glacial acetic acid (50 ml.) and ammonium acetate (4 g.) was refluxed for 3 hr. The solution was cooled and poured into ice-water. The precipitate was collected, washed and dried to yield the nitrostyrene (12 g.) which crystallised from dilute acetic acid in yellow needles, m.p. 78–79° (Found: C, 59·0; H, 6·1; N, 6·6. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·8; N, 6·3%).

2 : 4-Dimethoxybenzaldehyde (15 g.) was treated similarly with nitroethane (15 ml.), ammonium acetate (6 g.) and acetic acid (60 ml.) to yield 2 : 4-dimethoxy-β-methylnitrostyrene (18 g.), light yellow crystals from dilute acetic acid, m.p. 83° (Found: C, 59·2; H, 5·8; N, 6·3%).

By a similar procedure was obtained 2 : 5-dimethoxynitrostyrene, m.p. 120°, 2 : 3-dimethoxynitrostyrene, m.p. 88° and 2 : 4-dimethoxynitrostyrene, m.p. 108°. The melting points were in agreement with those reported in literature.

β-Phenylethylamines.—The following procedure illustrated in the case of β-(2 : 4-dimethoxyphenyl) isopropyl amine was adopted for all the amines, except β-(2 : 3-dimethoxyphenyl) isopropyl amine:

A solution of 2 : 4-dimethoxy-β-methylnitrostyrene (9 g.) in ether (150 ml.) was dropped into a suspension of lithium aluminum hydride (4 g.) in ether (150 ml.) during 2 hr. After stirring for 1 more hr., water was added to decompose the reaction mixture and the ether decanted off and extracted with hydrochloric acid (3 × 50 ml.; 2 N). The combined acid extracts were made basic with aqueous sodium hydroxide and extracted with ether. The ether extract was dried over potassium hydroxide and evaporated. The residue was distilled *in vacuo* to yield β-(2 : 4-dimethoxyphenyl) isopropyl amine

(4·5 g.), b.p. 147°/4 mm., $n^{30°}$ 1·512, yielding a hydrochloride, colourless needles from alcohol-ether, m.p. 147°.

β-(2: 5-Dimethoxyphenyl) ethyl amine, b.p. 160°/10 mm., $n^{30°}$ 1·524, β-(2: 5-dimethoxyphenyl) isopropyl amine, b.p. 148°/3 mm., β-(2: 3-dimethoxyphenyl) ethyl amine, b.p. 136–138°/5 mm., and β-(2:4-dimethoxyphenyl) ethyl amine, b.p. 143°/3 mm., $n^{30°}$ 1·344 were thus obtained from the corresponding nitrostyrenes.

The following procedure was adopted for β-(2: 3-dimethoxyphenyl)-isopropyl amine:

2: 3-*Dimethoxy-α-methylcinnamic acid.*—A mixture of 2: 3-dimethoxybenzaldehyde (40 g.), propionic anhydride (32 ml.) and fused sodium propionate (24 g.) was heated at 145° for 48 hr. The mixture was treated with a slight excess of 4 N sodium hydroxide, boiled and filtered. The cooled filtrate was shaken with benzene (3 × 60 ml.) and then acidified with concentrated hydrochloric acid. Crystallisation of the precipitate (41 g.) from alcohol gave 2: 3-dimethoxy-α-methylcinnamic acid, m.p. 113° (Found: C, 64·6; H, 6·4. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

β-(2: 3-*Dimethoxyphenyl*)-α-*methylpropionic acid.*—The above cinnamic acid (30 g.) was dissolved in the calculated quantity of N sodium hydroxide and reduced with sodium amalgam (5%; 500 g.) added in portions, with occasional additions of hydrochloric acid to keep the medium neutral. The aqueous layer was separated and acidified. The precipitated oil gradually solidified to give the propionic acid (28 g.), which crystallised from petroleum ether, melted at 57° (Found: C, 64·4; H, 7·1. $C_{12}H_{16}O_4$ requires C, 64·3, H, 7·1%).

β-(2: 3-*Dimethoxyphenyl*)-α-*methylpropionamide.*—A solution of the above acid (44 g.) in dry benzene (150 ml.) was left aside with thionyl chloride (32 ml.) for 24 hr., and poured into liquor ammonia (700 ml.) containing sodium hydroxide (10 g.) with stirring at 0°. Stirring was continued for 1hr., after the addition was over. The solid (34g.) that separated was filtered, washed and dried. On recrystallising from hot water, the amide melted at 85° (Found: C, 64·6; H, 7·0, N, 6·3. $C_{12}H_{17}O_3N$ requires C, 64·6; H, 7·6; N, 6·3%).

β-(2: 3-*Dimethoxyphenyl) isopropyl amine.*—The above amide (7·5 g.) in dioxane (30 ml.) was added at 0° to sodium hypochlorite solution (prepared by passing chlorine from 3 g. potassium permanganate into 12 g. sodium hydroxide dissolved in 100 g. ice and 20 g. water) and stirred at 0° for 1 hr. The solution was warmed to 50°, treated with solid potassium hydroxide (25 g.) and maintained at 70° for 1 hr. It was then cooled and

extracted with benzene. The benzene layer was shaken with hydrochloric acid (250 ml.; 1 N). The acid layer was separated, cooled, basified and extracted with ether. The ether layer was dried, and evaporated and the residue distilled *in vacuo* to give the isopropyl amine (1·5 g.), b.p. 125°/1 mm., yielding a hydrochloride, which on crystallisation from alcohol-ether, melted at 154°.

β-Phenylethylamides.—Formyl derivatives were made by heating the amine with 95% formic acid for 3 hr., at 180°, and isolating the neutral product. Acetyl derivatives were obtained by refluxing the amine for ½–1 hr., with acetic anhydride and dilution with ice-water. Benzoyl and phenylacetyl derivatives were obtained by the Schotton-Baumen procedure, using the appropriate acid chloride.

The formyl and acetyl derivatives of β-(2: 3-dimethoxyphenyl)-ethyl and isopropylamines were obtained as oils and were used as such for cyclisation. The other amides are listed in Table I.

3: 4-*Dihydroisoquinolines.*—The procedure adopted for cyclisation of the amides is illustrated in the case of N-acetyl-β-(2: 5-dimethoxyphenyl)-ethyl amine.

A solution of the acetamide (0·95 g.) in dry toluene (9 ml.) and phosphorus oxychloride (4 ml.) was refluxed for 2 hr., and poured into crushed ice. After some time, the aqueous layer was separated, and the toluene extracted with hydrochloric acid (10 ml.; 4 N). The combined acid extracts were shaken once with ether, cooled, basified and extracted with ether. The ether extract was dried over anhydrous potassium carbonate and evaporated to yield the dihydroisoquinoline (0·76 g.) as a yellow oil which solidified on standing.

The dihydroisoquinolines were characterised mainly as the picrates; some of them were obtained as solids by crystallisation or vacuum sublimation. Table II records relevant data.

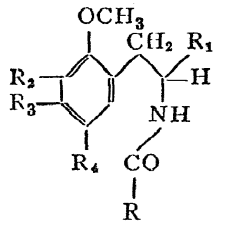
None of the derivatives of β-(2: 4-dimethoxyphenyl) ethyl- and isopropyl amines could be cyclised.

Isoquinolines.—The procedure used for dehydrogenating the dihydroisoquinolines is illustrated in the case of 3: 4-dihydro-5: 8-dimethoxy-3-methylisoquinoline.

The dihydroisoquinoline (0·3 g.) was dissolved in decalin (50 ml.) and heated with palladised charcoal (5%, 0·1 g.) at 180–90° for 7 hr., in an atmosphere of carbon dioxide till no more hydrogen was evolved. The

TABLE I

β-Phenylethylamides

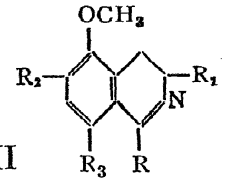


I

R	R_1	R_2	R_3	R_4	Molecular formula	M.P. ° C.	Found %			Required %		
							C	H	N	C	H	N
H	H	H	H	OMe	$C_{11}H_{15}O_3N$	70	62·7	7·0	6·8	63·1	7·2	6·7
Me	H	H	H	OMe	$C_{12}H_{17}O_3N$	99–100[9]	..	..	..	..	..	..
Ph	H	H	H	OMe	$C_{17}H_{19}O_3N$	86	71·4	6·4	5·0	71·6	6·7	4·9
$PhCH_2$	H	H	H	OMe	$C_{12}H_{21}O_3N$	105	72·4	7·2	4·9	72·2	7·0	4·7
H	Me	H	H	OMe	$C_{19}H_{17}O_3N$	78	64·4	7·5	6·3	64·6	7·6	6·3
Me	Me	H	H	OMe	$C_{13}H_{19}O_3N$	111–112[10]	..	..	6·2	..	..	6·2
Ph	Me	H	H	OMe	$C_{18}H_{21}O_3N$	155–156	72·3	7·2	4·5	72·2	7·0	4·9
$PhCH_2$	Me	H	H	OMe	$C_{19}H_{23}O_3N$	137	73·2	6·9	4·5	72·9	7·3	4·5
Ph	H	OMe	H	H	$C_{17}H_{19}O_3N$	86	71·3	6·7	4·8	71·6	6·7	4·9
$PhCH_2$	H	OMe	H	H	$C_{18}H_{21}O_3N$	112	72·4	7·2	4·5	72·2	7·0	4·7
Ph	Me	OMe	H	H	$C_{18}H_{21}O_3N$	70	72·6	6·8	4·9	72·2	7·0	4·7
$PhCH_2$	Me	OMe	H	H	$C_{19}H_{23}O_3N$	81	72·5	7·5	4·5	72·9	7·3	4·6
Ph	H	H	OMe	H	$C_{17}H_{19}O_3N$	115	..	..	5·0	..	..	4·9
$PhCH_2$	H	H	OMe	H	$C_{18}H_{21}O_3N$	134	..	..	4·7	..	..	4·7
Me	Me	H	OMe	H	$C_{13}H_{19}O_3N$	96	65·7	7·7	6·0	65·8	8·0	5·9
Ph	Me	H	OMe	H	$C_{18}H_{21}O_3N$	132	72·1	6·9	4·7	72·2	7·0	4·7
$PhCH_2$	Me	H	OMe	H	$C_{19}H_{23}O_3N$	120	72·3	7·2	4·6	72·9	7·3	4·5

TABLE II

Picrates of 3 : 4-*Dihydroisoquinolines*



II

R	R_1	R_2	R_3	Molecular formula	M.P. ° C.	Found %			Required %		
						C	H	N	C	H	N
H	H	H	OMe	$C_{17}H_{16}O_9N_4$	160	48·8	3·7	13·5	48·6	3·8	13·3
Me	H	H	OMe	$C_{18}H_{18}O_9N_4$[a]	189	49·3	4·5	13·1	49·7	4·1	12·9
Ph	H	H	OMe	$C_{23}H_{20}O_9N_4$[b]	195	55·8	3·8	11·5	55·6	4·0	11·3
$PhCH_2$	H	H	OMe	$C_{24}H_{22}O_9N_4$	165	56·5	4·3	11·1	56·5	4·3	11·0
H	Me	H	OMe	$C_{18}H_{18}O_9N_4$	203	49·4	3·7	13·2	49·8	4·1	12·9
Me	Me	H	OMe	$C_{23}H_{25}O_7N_5$[c]	186	..	..	14·8	..	..	14·5
Ph	Me	H	OMe	$C_{24}H_{22}O_9N_4$[d]	181	56·9	4.2	11·1	56·5	4·3	11·0
$PhCH_2$	Me	H	OMe	$C_{25}H_{24}O_9N_4$	152	56·9	4·4	10·7	57·3	4·6	10·7
H	H	OMe	H	$C_{17}H_{16}O_9N_4$	185	48·8	3·6	13·3	48.6	3·8	13·3
Me	H	OMe	H	$C_{22}H_{23}O_7N_5$[e]	234	56·5	5·3	14·8	56·3	4·9	14·9
Ph	H	OMe	H	$C_{23}H_{20}O_9N_4$[f]	162	55·8	3·7	11·5	55·6	4·0	11·3
$PhCH_2$	H	OMe	H	$C_{24}H_{22}O_9N_4$	172	56·1	4.4	10·8	56·5	4·3	11·0
H	Me	OMe	H	$C_{18}H_{18}O_9N_4$	182	50·0	4·1	12·8	49·8	4·1	12·9
Me	Me	OMe	H	$C_{19}H_{20}O_9N_4$	146	51·1	4·8	12·7	50·9	4·5	12·5
Ph	Me	OMe	H	$C_{24}H_{22}O_9N_4$	149	56·1	4·2	11·1	56·5	4·3	11·0
$PhCH_2$	Me	OMe	H	$C_{25}H_{24}O_9N_4$	149	57·2	4·4	10·7	57·3	4·6	10·7

[a] Free base, m.p. 68° (*cf.* Sugasawa and Shigehara[9]).
[b] Free base, m.p. 99° (Found: C, 76·7; H, 6·4; N, 5·4. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%).
[c] Picrolonate; hydrochloride, m.p. 177° (*cf.* Govindachari and Pai[4]).
[d] Base, m.p. 129° (Found: C, 77·1; H, 6·9; N, 4·9. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8; N, 4·9%); hydrochloride, m.p. 2 05°. (decomp.) (Found: C, 67·9; H, 6·4; N, 4·4. $C_{18}H_{20}O_2NCl$ requires C, 68·0; H, 6·3; N, 4·4%).
[e] Picrolonate; picrate, m.p. 215° (decomp.) (*cf.* Rajagopalan[10]).
[f] Base, m.p. 105° (Found: C, 75·9; H, 6·4; N, 5·5. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%).

TABLE

Iso

R	R_1	R_2	R_3	BASE						
				Molecular Formula	M.P. °C.	Found %			Required %		
						C	H	N	C	H	N
H ..	H	H	OMe	$C_{11}H_{11}O_2N$	58	69·5	5·9	..	69·8	5·8	..
Me ..	H	H	OMe	$C_{12}H_{13}O_2N$	54	70·9	6·2	..	70·9	6·4	..
Ph ..	H	H	OMe	$C_{17}H_{15}O_2N$	124	76·7	5·7	5·4	77·0	5·7	5·3
$PhCH_2$	H	H	OMe	$C_{18}H_{17}O_2N$	89	77·9	6·2	5·1	77·4	6·1	5·0
H ..	Me	H	OMe	$C_{12}H_{13}O_2N$	77	71·1	6·2	..	70·9	6·4	..
Me ..	Me	H	OMe	$C_{13}H_{15}O_2N \cdot H_2O$	70	66·0	7·2	6·0	66·4	7·2	6·0
Ph ..	Me		OMe	$C_{18}H_{17}O_2N$	118	77·0	6·0	5·2	77·4	6·1	5·0
$PhCH_2$	Me	H	OMe	$C_{19}H_{19}O_2N$	114	78·2	6·8	4·8	77·8	6·5	4·8
H ..	H	OMe	H	$C_{11}H_{11}O_2N$	40	..	..	..	..	..	..
Me ..	H	OMe	H	$C_{12}H_{13}O_2N$	93	70·4	6·1	7·2	70·9	6·4	6·9
Ph ..	H	OMe	H	$C_{17}H_{15}O_2N$	112	77·2	5·6	5·3	77·0	5·7	5·3
$PhCH_2$	H	OMe	H	..	..	..	..	..	..	..	..
H ..	Me	OMe	H	$C_{12}H_{13}O_2N$	85	70·5	6·6	7·1	70·9	6·4	6·9
Me ..	Me	OMe	H	..	..	..	..	..	..	..	..
Ph ..	Me	OMe	H	$C_{18}H_{17}O_2N$	85	77·1	6·2	..	77·4	6·0	..
$PhCH_2$	Me	OMe	H	$C_{19}H_{19}O_2N$	134	77·5	6·8	4·9	77·8	6·5	4·8

[a] Picrolonate; Base hydrochloride, m.p. 234° (Found: C, 57·4; H, 6·9; N, 5·5.

[b] Base hydrochloride, m.p. 166° (Found: C, 67·8; H, 5·7; $C_{18}H_{18}O_2NCl$ requires C, 68·3;

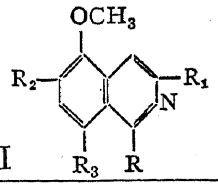
[c] Base hydrochloride, m.p. 209° (decomp.) (Found: C, 68·6; H, 6·3; N, 3·9. $C_{19}H_{20}O_2NCl$

[d] Picrolonate.

decalin solution was filtered and the catalyst washed with benzene (10 ml). The combined filtrates were repeatedly extracted with hydrochloric acid (3×25 ml.; 4 N). The acid extracts were cooled, basified and extracted with ether. The ether extract was dried and evaporated to leave the isoquinoline (0·2 g.).

III

quinolines



III

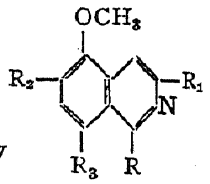
PICRATE

Mol. Formula	M.P. °C.	Found %			Required %		
		C	H	N	C	H	N
$C_{17}H_{14}O_9N_4$	210 (decomp.)	..	..	13·3	..	..	13·4
$C_{18}H_{16}O_9N_4$	237 (decomp.)	50·4	3·4	12·7	50·0	3·7	12·9
$C_{23}H_{18}O_9N_4$	202	56·2	3·6	11·3	55·9	3·6	11·3
$C_{24}H_{20}O_9N_4$	215	56·3	4·1	11·1	56·7	3·9	11·0
$C_{18}H_{16}O_9N_4$	243 (decomp.)	49·7	3·9	12·9	50·0	3·7	12·9
$C_{23}H_{23}O_7N_5 \cdot H_2O$[a]	230	..	..	13·8	..	..	14·0
$C_{24}H_{20}O_9N_4$[b]	178	57·2	4·0	..	56·7	3·9	..
$C_{25}H_{22}O_9N_4$[c]	176	56·9	3·9	10·4	57·5	4·2	10·7
$C_{17}H_{14}O_9N_4$	211	48·5	3·2	13·0	48·8	3·3	13·4
$C_{22}H_{21}O_7N_5$[d]	245	56·9	5·0	15·0	56·5	4·5	15·0
$C_{23}H_{18}O_9N_4$	168	55·5	3·8	11·2	55·9	3·6	11·3
$C_{24}H_{20}O_9N_4$	208	56·4	3·7	11·0	56·7	3·9	11·0
$C_{18}H_{16}O_9N_4$	241	50·1	3·5	13·3	50·0	3·7	13·0
$C_{19}H_{18}O_9N_4$[e]	184	50·8	3·8	12·5	51·1	4·0	12·6
$C_{24}H_{20}O_9N_4$	180	56·6	4·2	10·7	56·7	3·9	11·0
$C_{25}H_{22}O_9N_4$	162	57·8	4·0	..	57·5	4·2	..

$C_{13}H_{16}O_2NCl \cdot H_2O$ requires C, 57·5; H, 6·6; N, 5·2%); (*cf.* Govindachari and Pai[4]).
H, 5·7%).
requires C, 68·7; H, 6·0; N, 4·2%).
[e] *cf.* Govindachari and Pai[4].

Palladised charcoal in decalin at 210–40° was used for dehydrogenating dihydroisoquinolines with a substituent at 1-position and none at 3. For 1 : 3-unsubstituted dihydroisoquinolines, palladium black in decalin at 200° was required. The isoquinolines were purified by crystallisation or sublimation or regeneration from pure derivatives. In this manner all the

isoquinolines except 5:6-dimethoxy-, 5:6-dimethoxy-3-methyl-, and 5:6-dimethoxy-1:3-dimethylisoquinolines were obtained as crystalline solids. The appropriate data are summarised in Table III. The u.v. absorption data are recorded in Table IV.



IV

TABLE IV

R	R_1	R_2	R_3	λ_{max} in mμ	log ϵ_{max}
H	H	H	OMe	220, 240, 245, 250, *276–277*, 283, 320, 330, 350	4·3, 4·22, 4·26, 4·17, 3·88, 3·81, 3·99, 3·86, 3·88
Me	H	H	OMe	245, 335	4·07, 3·83
Ph	H	H	OMe	214·5, 322, 325	4·4, 3·79, 3·82
$PhCH_2$	H	H	OMe	*248–249*, 335	4·21, 3·84
H	Me	H	OMe	225, 249–250, 325, *346–348*, 350	4·27, 4·24, 3·62, 3·71, 3·71
Me	Me	H	OMe	225, 250, 315, 345	4·12, 4·04, 3·77, 3·81
Ph	Me	H	OMe	253, 320, *322–325*, *352–354*	4·14, 3·85, 3·85, 3·85
$PhCH_2$	Me	H	OMe	254, *319–322*, 350	4·16, 3·78, 3·79
H	H	OMe	H	*237–238*, 255, 300, 310, 365	4·72, 3·73, 3·68, 3·67, 2·55
Me	H	OMe	H	240, 305	4·64, 3·70
Ph	H	OMe	H	230, 234, 236, *310–315*	4·50, 4·55, 4·65, 3·82
$PhCH_2$	H	OMe	H	236, 238, 241, 244, 305	4·67, 4·68, 4·66, 4·68, 3·79
H	Me	OMe	H	236, 238, *240–241*, 305	4·71, 4·73, 4·71, 3·65
Me	Me	OMe	H	241, 243, 304	4·64, 4·64, 3·63
Ph	Me	OMe	H	231, 235, 311, *316–318*, 330	4·56, 4·65, 3·86, 3·84, 3·84
$PhCH_2$	Me	OMe	H	242, 246, *310–315*	4·69, 4·69, 3·67

SUMMARY

A series of 3:4-dihydro-5:6-dimethoxy and 3:4-dihydro-5:8-dimethoxyisoquinolines are reported. These have been dehydrogenated to the corresponding isoquinoline derivatives.

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REFERENCES

1. *Chem. Zentr.*, 1931, **102**, II, 1196, B.P. 348956.
2. G.P. 61,3005.
3. Burger .. *Medicinal Chemistry*, Interscience Publishers, Inc., 1, 409.
4. Govindachari and Pai .. *J. Org. Chem.*, 1953, **18**, 1253.
5. Buck and Baltzly .. *J. Amer. Chem. Soc.*, 1940, **62**, 161.
6. ——— .. *Ibid.*, 164.
7. Späth, Riedl and Kubiezek .. *Monatsh*, 1948, **79**, 72.
8. Whaley and Govindachari .. *Organic Reactions*, **6**, 74.
9. Sugasawa and Shigehara .. *Ber.*, 1941, **74**, 459.
10. Rajagopalan .. *Proc. Ind. Acad. Sci.*, 1941, **13 A**, 566.