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An Abnormal Formation of Indane from N-Phenethylphenylpropionamide under Bischler-Napieralski Reaction Conditions

Tetsuji Kametani, Yoshinari Satoh, and Keiichiro Fukumoto

Pharmaceutical Institute, Tohoku University[1]

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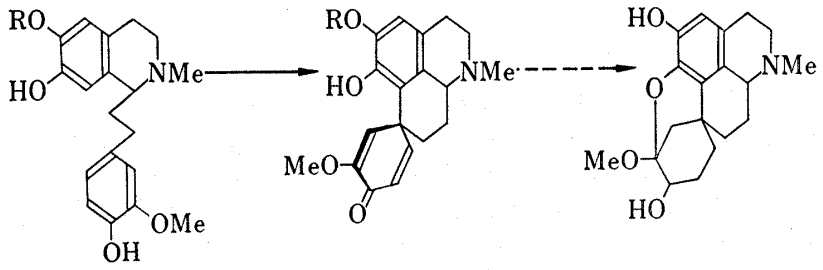
A treatment of N-(3-acetoxy-4-benzyloxyphenethyl)-4-benzyloxy-3-methoxyphenylpropionamide (**17**) with phosphoryl chloride gave 1-(3-acetoxy-4-benzyloxyphenethyl)-imino-6-benzyloxy-5-methoxyindane (**21**) instead of the normal product, 3,4-dihydroisoquinoline (**20**). The structure of **21** was determined by chemical method and by an alternative synthesis of the indane derivative (**25**) derived from **21**.

Keywords——abnormal formation of indane; N-phenethylphenylpropionamide; Bischler-Napieralski reaction; 1-(3-acetoxy-4-benzyloxyphenethyl)imino-6-benzyloxy-5-methoxyindane; kesselringine

In a previous paper,[2] we have reported a synthesis of the homoproaporphine (**5**), which would be a key intermediate to an alkaloid kesselringine (**9**),[3] by a phenol oxidation of the triphenolic phenethylisoquinoline (**1**). However, this reaction proceeded in poor yield, the result of which would be ascribable to the fact that the starting isoquinoline (**1**) or the product (**5**) has an unstable catechol ring system in the air and a tendency to an undesirable coupling reaction. On the other hand, the kreysiginone (**6**), in which one hydroxyl group in **5** is replaced by methoxyl group, is obtained from the diphenolic isoquinoline (**2**) in good yield by the same reaction.[4] Therefore we planned a synthesis of the homoproaporphines (**7** and **8**) by a phenol oxidation of 6-acetoxy- or 6-mesyloxy-1,2,3,4-tetrahydro-7-hydroxy-1-(4-hydroxy-3-methoxyphenethyl)-2-methylisoquinolines (**3** and **4**) in which an unnecessary hydroxyl group to the oxidative coupling in catechol system is protected by acetyl or mesyl group.



1: R=H
2: R=Me
3: R=COMe
4: R=SO_2Me

5: R=H
6: R=Me
7: R=COMe
8: R=SO_2Me

9

Chart 1

During a synthetic process of the starting isoquinolines (**3** and **4**), we have found an abnormal formation of the indane (**21**) in the Bischler-Napieralski reaction of the amide (**17**), and we here report on this interesting but abnormal result.

1) Location: *Aobayama, Sendai 980, Japan.*
2) T. Kametani, Y. Satoh, and K. Fukumoto, *Chem. Pharm. Bull.* (Tokyo), **25**, 922 (1977).
3) M.K. Jusupov, *Chim. Rastitel, Vecěstv, Jašhent*, **1972**, 19; this literature was given by Professor Šantavý as a private communication.
4) T. Kametani, F. Satoh, H. Yagi, and K. Fukumoto, *J. Org. Chem.*, 33, 690 (1968).

Methoxymethylation of 4-benzyloxy-3-hydroxybenzaldehyde (**10**)[5] with chloromethyl methyl ether in benzene in the presence of sodium hydride gave, in 78% yield, the methoxymethyl ether (**11**), which was converted into the corresponding nitrostyrene (**12**) in 58% yield by a treatment with nitromethane in the presence of methylamine. Reduction of **12** with lithium aluminum hydride in boiling tetrahydrofuran afforded in 57% yield the phenethylamine (**13**), which was condensed with 4-benzyloxy-3-methoxyphenylpropionic acid (**14**)[6] by heating to give the amide (**15**) in 63% yield. Bischler-Napieralski reaction of **15** under several conditions did not provide the expected 3,4-dihydroisoquinoline (**18**) but a tar. Similarly, the phenolic amide (**16**), obtained by a treatment of **15** with methanolic hydrochloric acid, with phosphoryl chloride gave a complicated mixture but not the isoquinoline (**19**).

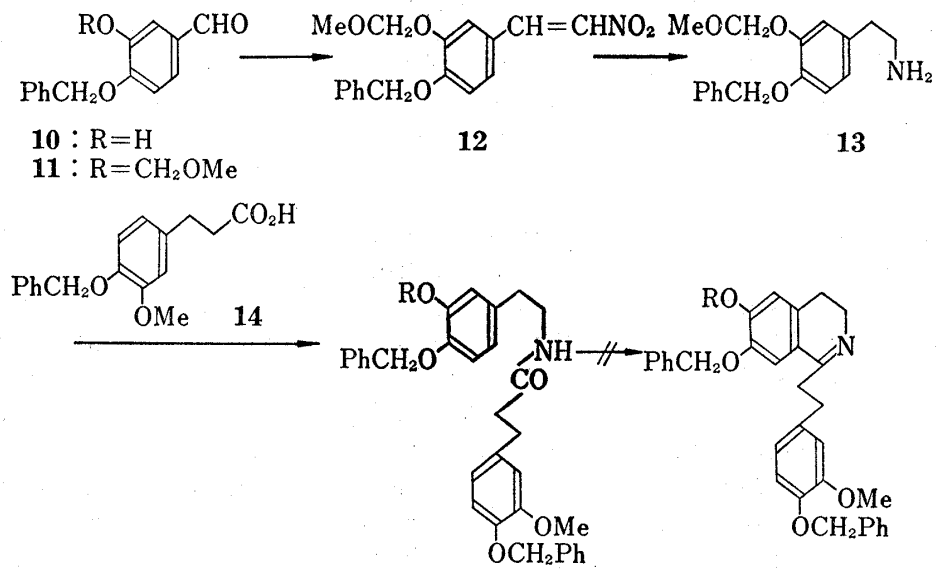


Chart 2

Secondly, we have examined a cyclization of the N-(3-acetoxy-4-benzyloxyphenethyl)-phenylpropionamide (**17**), prepared from **16** by an acetylation with acetyl chloride and triethylamine, to the 3,4-dihydroisoquinoline (**20**). The reaction of the amide (**17**) with phosphoryl chloride in boiling benzene gave the starting material unchanged, but the same reaction in boiling acetonitrile afforded surprisingly the unexpected indane derivative (**21**), which was characterized as methiodide (**22**), mp 116—118°, in 48% yield. Evidence which completed the structural assignments as depicted in **22** came from reduction studies. Thus, sodium borohydride reduction of **22** provided the 1-(N-methyl-N-phenethyl)aminoindane (**23**) in 73% yield. The structure of the latter was elucidated from the fact that the presence of indane system and N-methyl-N-phenethyl group was revealed by the ions at *m/e* 297, 268 and 252 (base peak) which corresponded to **29**, **30** and **31**, respectively, in its mass spectrum [*m/e* 551 (M^+)]. Moreover, a treatment of the phenolic base (**24**), obtained by mild hydrolysis of **23** with methanolic potassium hydroxide, with mesyl chloride in chloroform in the presence of triethylamine caused a Hofmann type elimination to give the known indene (**28**), mp 83—85° (lit.,[7] 81—82°), whose nuclear magnetic resonance (NMR) spectrum showed

5) T. Kametani and K. Fukumoto, *Tetrahedron Letters*, **1964**, 2771.
6) R.E. Harmon and B.L. Jensen, *J. Heterocyclic Chem.*, **7**, 1077 (1970).
7) J. Sam and T.C. Snapp, *J. Pharm. Sci.*, **54**, 756 (1965).

three typical indene resonances,[8] namely C_1-H at 3.31 as triplet having $J=2$ Hz, C_2-H at 6.28—6.47 as multiplet and C_3-H at 6.62—6.82 as multiplet. Moreover, the appearance of two singlets (6.94 and 7.06) assigned to aromatic protons indicated the indene derivative to have the substituents at C_5 -and C_6-positions. Thus, the presence of an indane system in **23** is established and, in turn, the structure of the product formed by a reaction of the amide (**17**) with phosphoryl chloride is now also known with certainty.

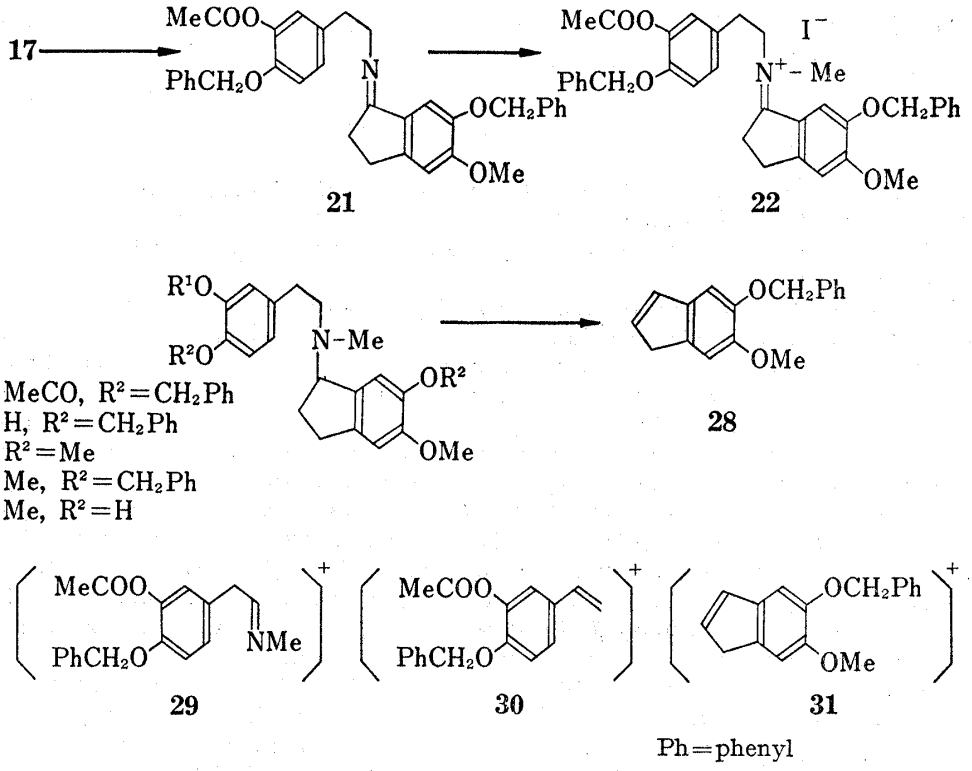


Chart 3

Furthermore, a confirmation of the structure having an indane ring was carried out by an alternative synthesis of **25**, which was prepared from **24** by methylation and then debenzylation of the nonphenolic base (**26**), followed by methylation of **27** with diazomethane. The Schiff bass (**34**), which was obtained by a condensation of the phenethylamine (**32**) with the indanone (**33**), was reduced with sodium borohydride to the secondary amine (**35**).

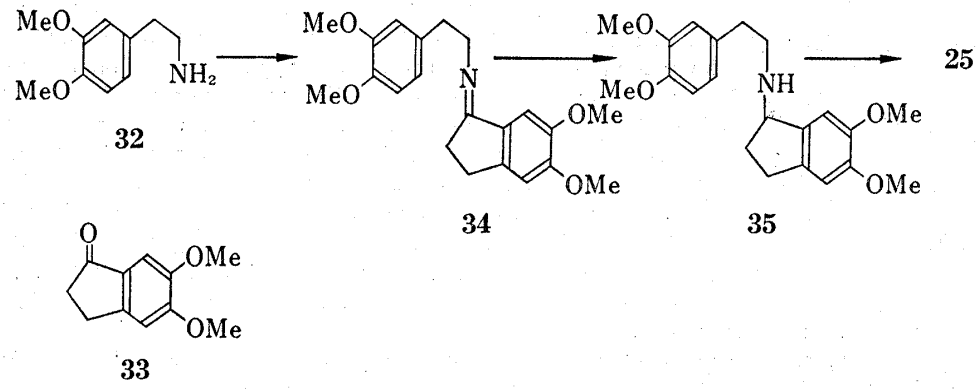


Chart 4

8) N.S. Bhacca, L.F. Johnson, and J.N. Schoolery, "NMR Spectra Catalog," No. 227, Varian Associates, Palo Alto, California, 1962.

Eschweiler-Clarke reaction of **35** with formalin and sodium borohydride gave the 1-aminoindane, which was identical with our product (**25**) in all respects in melting point and spectral comparisons. Thus, we confirmed the structure of the abnormal reaction product from the amide (**17**).

The abnormal formation of the indane derivative (**21**) from the amide (**17**) under Bischler-Napieralski reaction conditions would be due to the fact that the methoxylated aromatic ring is more reactive than the acetoxylated one in a reaction with the carbonium cation derived from amide carbonyl function, because an electron-donating effect of methoxyl group is stronger than of acetoxyl group.

Experimental

All melting points are uncorrected and were measured with a Yanagimoto micro melting point apparatus (MP-22). Infrared (IR) spectra were measured with a Hitachi 215 grating spectrophotometer, NMR spectra with a JEOL PMX−60 spectrometer with Me_4Si as an internal standard, and mass spectra with a Hitachi RMU-7 spectrometer.

4-Benzyloxy-3-methoxymethoxybenzaldehyde (**11**)——To a suspension of 4-benzyloxy-3-hydroxybenzaldehyde (**10**)[5] (53.0 g, 0.23 mole) in refluxing benzene (500 ml) was added 50% sodium hydride (13 g, 0.27 mole) with stirring in a current of nitrogen and the resulting mixture was stirred for 2 hr under reflux. After cooling, chloromethyl methyl ether (21.0 g, 0.26 mole) was added to the above reaction mixture with stirring at 0° in a current of nitrogen. The mixture was stirred at room temperature for 8 hr and then refluxed for 1 hr. After completion of the reaction, the mixture was poured into water and the organic layer was separated, washed with water and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* gave a yellow oil which was distilled to give the aldehyde (**11**) (49.0 g, 78%), bp 181—182° (0.08 mmHg). After solidification on standing in the air, it showed mp 56—57°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (>CO), NMR ($CDCl_3$) ppm: 3.43 (3H, s, OMe), 5.09 (2H, s, $OC\underline{H}_2Ph$), 5.14 (2H, s, OCH_2O), 6.91 (1H, d, $J=8$ Hz, C_5–H), 7.18—7.60 (2H, m, ArH) and 7.28 (5H, broad s, $OCH_2C_6\underline{H}_5$). *Anal.* Calcd. for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.61; H, 6.11.

4-Benzyloxy-3-methoxymethoxy-β-nitrostyrene (**12**)——To a mixture of the aldehyde (**11**) (49.0 g, 0.18 mole), ethanol (200 ml) and nitromethane (13.4 g, 0.22 mole) was added methylamine [prepared from methylamine hydrochloride (9.0 g)] at 10° and the mixture was allowed to stand at 0° for 2—4 days to give the nitrostyrene (**12**) (32.8 g, 58%) as pale yellow needles, mp 97.5—98°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1630 (>C=C<), NMR ($CDCl_3$) ppm: 3.56 (3H, s, OMe), 5.23 (2H, s, $OC\underline{H}_2Ph$), 5.28 (2H, s, OCH_2O), 7.13 (1H, d, $J=16$ Hz, $-CH=C\underline{H}NO_2$), 7.68 (1H, d, $J=16$ Hz, $-C\underline{H}=CHNO_2$) and 6.86—7.65 (8H, m, ArH). *Anal.* Calcd. for $C_{17}H_{17}O_5N$: C, 64.75; H, 5.43; N, 4.44. Found: C, 65.11; H, 5.39; N, 4.38.

4-Benzyloxy-3-methoxymethoxyphenethylamine (**13**)——To a suspension of lithium aluminum hydride (17.0 g, 0.45 mole) in dry tetrahydrofuran (300 ml) was added a solution of the nitrostyrene (**12**) (47.0 g, 0.15 mole) in tetrahydrofuran (300 ml) during 1 hr with stirring in a current of nitrogen. After refluxing for 1 hr with stirring, the reaction mixture was decomposed with an excess of 30% sodium hydroxide. The organic layer was separated and concentrated to leave a residue which was extracted with benzene. The extract was washed with water, dried over Na_2SO_4, and distilled *in vacuo* to leave the amine (**13**) as a pale yellow syrup. NMR ($CDCl_3$) ppm: 1.80 (2H, broad, $-NH_2$), 2.48—3.13 (4H, m, $2\times CH_2$), 3.52 (3H, s, OMe), 5.11 (2H, s, $OC\underline{H}_2Ph$), 5.20 (2H, s, OCH_2O), 6.61—7.09 (3H, m, ArH) and 7.21—7.60 (5H, m, $OCH_2C_6\underline{H}_5$). This was characterized as oxalate (32.0 g, 57%), colorless needles, mp 151—152°, from methanol–ether. *Anal.* Calcd. for $C_{17}H_{21}O_3N\cdot C_2H_2O_4$: C, 60.47; H, 6.14; N, 3.71. Found: C, 60.18; H, 6.27; N, 3.57.

N-(4-Benzyloxy-3-methoxymethoxyphenethyl)-4-benzyloxy-3-methoxyphenylpropionamide (**15**)——A mixture of the amine (**13**) (14.8 g, 52 mmole) and 4-benzyloxy-3-methoxyphenylpropionic acid (**14**)[6] (14.3 g, 50 mmole) was heated at 170—180° for 2 hr in a current of nitrogen. After cooling, the reaction mixture was taken up in benzene and the extract was washed with 10% hydrochloric acid, saturated sodium bicarbonate solution, and water, and dried over K_2CO_3. Evaporation of the solvent *in vacuo* gave the amide (**15**) (17.4 g, 63%) as colorless needles, mp 89—90°, from benzene–*n*-hexane. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (>NH) and 1650 (>CO), NMR ($CDCl_3$) ppm: 2.18—3.10 (6H, m, $3\times CH_2$), 3.20—3.61 (2H, m, $CH_2C\underline{H}_2N$), 3.47 (3H, s, $OCH_2-O\underline{CH}_3$), 3.82 (3H, s, ArOMe), 5.06 (4H, s, $2\times OC\underline{H}_2Ph$), 5.15 (2H, s, OCH_2O), 5.19—5.54 (1H, m, NH), 6.43—6.98 (6H, m, ArH) and 7.11—7.58 (10H, m, $2\times OCH_2C_6\underline{H}_5$). *Anal.* Calcd. for $C_{34}H_{37}O_6N$: C, 73.49; H, 6.71; N, 2.52. Found: C, 73.83; H, 6.89; N, 2.61.

N-(4-Benzyloxy-3-hydroxyphenethyl)-4-benzyloxy-3-methoxyphenylpropionamide (**16**)——To a solution of the above amide (**15**) (16.6 g, 30 mmole) in methanol (30 ml) was added dropwise concentrated hydrochloric acid (10 ml) with stirring at 0°. After stirring for 2 hr at room temperature, the reaction mixture was basified with 10% ammonia and the separated oil was extracted with chloroform. The extract was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to give the phenolic amide (**16**) (12.5 g, 82%) as colorless needles, mp 132—133°, from benzene. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (–OH), 3450 (>NH) and 1650 (>CO), NMR ($CDCl_3$) ppm: 2.12—3.07 (6H, m, $3\times CH_2$), 3.18—3.62 (2H, m, $C\underline{H}_2CH_2N$), 3.84 (3H, s, OMe), 5.03

(2H, s, $OC\underline{H}_2Ph$), 5.07 (2H, s, $OC\underline{H}_2Ph$), 5.20—5.52 (1H, m, NH), 5.76 (1H, broad s, OH), 6.36—6.91 (6H, m, ArH) and 7.13—7.55 (10H, m, $2\times OCH_2C_6\underline{H}_5$). *Anal.* Calcd. for $C_{32}H_{33}O_5N$: C, 75.12; H, 6.50; N, 2.74. Found: C, 75.20; H, 6.82; N, 2.78.

N-(3-Acetoxy-4-benzyloxyphenethyl)-4-benzyloxy-3-methoxyphenylpropionamide (17)——Acetyl chloride (2.0 g, 25 mmole) was added dropwise to a mixture of the phenolic amide (**16**) (11.2 g, 22 mmole), triethylamine (3.0 g, 30 mmole) and chloroform (40 ml) with stirring at 0°. After stirring for 2 hr at room temperature, the reaction mixture was washed with 10% hydrochloric acid and water, and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* gave the nonphenolic amide (**17**) (11.0 g, 90%) as colorless needles, mp 137—138°, from ethanol. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (>NH), 1750 (–OCOMe) and 1650 (–CO–N<), NMR ($CDCl_3$) ppm: 2.24 (3H, s, COMe), 2.15—3.08 (6H, m, $3\times CH_2$), 3.21—3.62 (2H, m, $CH_2C\underline{H}_2N$), 3.82 (3H, s, OMe), 5.02 (2H, s, $OC\underline{H}_2Ph$), 5.08 (2H, s, $OC\underline{H}_2Ph$), 5.28—5.63 (1H, m, NH), 6.41—6.95 (6H, m, ArH) and 7.07—7.56 (10H, m, $2\times OCH_2C_6\underline{H}_5$). *Anal.* Calcd. for $C_{34}H_{35}O_6N$: C, 73.76; H, 6.37; N, 2.53. Found: C, 73.62; H, 6.44; N, 2.42.

Reaction of the Amide (17) with Phosphoryl Chloride——To a solution of the above amide (**17**) (6.6 g, 12 mmole) in acetonitrile (50 ml) was added phosphoryl chloride (15 g) under reflux and the mixture was further refluxed for 8 hr. After evaporation of the solvent and reagent *in vacuo*, the residue was washed with ether, basified with 10% ammonia and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4 and distilled *in vacuo* to leave the indane (**21**) as a pale brown syrup, to which was added methyl iodide (20 ml). The mixture was allowed to stand overnight at room temperature and then an excess of methyl iodide was distilled off. The residue was washed with ether to give the methiodide (**22**) (3.8 g, 48%) as colorless needles, mp 116—118°, from acetone. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (>CO) and 1630 (>C=$\overset{+}{N}$<), Mass Spectrum *m/e*: 550 M^+-I^-), 281, 268, 252 and 226. *Anal.* Calcd. for $C_{35}H_{36}O_5NI$: C, 62.04; H, 5.36; N, 2.06. Found: C, 62.37; H, 5.43; N, 1.99.

1-[N-(3-Acetoxy-4-benzyloxyphenethyl)-N-methyl]amino-6-benzyloxy-5-methoxyindane (23)——Sodium borohydride (1 g) was added in small portions to a suspension of the methiodide (**22**) (3.4 g, 5.0 mmole) in methanol (80 ml) with stirring at 0—5° and then stirring was continued for 1 hr at 0—5°. After adjusting pH of the reaction mixture to 5—6 by addition of a few drops of concentrated hydrochloric acid, methanol was distilled off *in vacuo*. The residue was taken up in chloroform and the extract was washed with 10% ammonia and sodium chloride solution, and dried over Na_2SO_4. The solvent was distilled *in vacuo* to leave a residue, which was chromatographed on silica gel (60 g) by elution with chloroform to give the indane (**23**) (2.0 g, 73%) as a pale yellow viscous syrup. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790 (>NMe) and 1755 (>CO), NMR ($CDCl_3$) ppm: 2.21 (3H, s, COMe), 2.23 (3H, s, NMe), 3.83 (3H, s, OMe), 4.39 (1H, m, C_1–H), 5.01 (2H, s, $OC\underline{H}_2Ph$), 5.10 (2H, s, $OC\underline{H}_2Ph$), 6.58—6.96 (5H, m, ArH) and 7.12—7.53 (10H, m, $2\times OCH_2C_6\underline{H}_5$), Mass Spectrum *m/e*: 551 (M^+), 297, 268 and 252 (base peak).

5-Benzyloxy-6-methoxyindene (28)——A mixture of the indane (**23**) (820 mg, 1.5 mmole), 2N potassium hydroxide (1 ml) and methanol (5 ml) was refluxed for 10 min, and then methanol was evaporated *in vacuo*. The residue was treated with saturated ammonium chloride solution and extracted with chloroform. The extract was washed with saturated ammonium chloride solution, dried over Na_2SO_4 and evaporated to give the phenolic indane (**24**) as a pale yellow syrup. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (–OH) and 2800 (>NMe), NMR ($CDCl_3$) ppm: 2.25 (3H, s, NMe), 3.80 (3H, s, OMe), 4.45 (1H, m, C_1–H), 4.95 (2H, s, $OC\underline{H}_2Ph$), 5.07 (2H, s, $OC\underline{H}_2Ph$), 6.42—7.01 (5H, m, ArH) and 7.12—7.92 (10H, m, $2\times OCH_2C_6\underline{H}_5$).

To a solution of **24** and triethylamine (400 mg, 4 mmole) in chloroform (30 ml) was added slowly mesyl chloride (400 mg, 3.5 mmole) with stirring at 0° and the stirring was continued for 5 hr at room temperature. The reaction mixture was washed with saturated sodium bicarbonate solution and water, dried over Na_2SO_4 and distilled off *in vacuo* to leave a syrup, which was subjected to silica gel (15 g) chromatography. The chloroform eluate gave 5-benzyloxy-6-methoxyindene (**28**) (150 mg) as colorless prisms, mp 83—85° (lit.,[7] mp 81—82°), from ethanol. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1610 (>C=C<), NMR ($CDCl_3$) ppm: 3.31 (2H, t, $J=2$ Hz, C_1–H), 3.88 (3H, s, OMe), 5.16 (2H, s, $OC\underline{H}_2Ph$), 6.28—6.47 (1H, m, C_2–H), 6.62—6.82 (1H, m, C_3–H), 6.94 (1H, s, ArH), 7.06 (1H, s, ArH) and 7.18—7.56 (5H, m, $OCH_2C_6\underline{H}_5$).

1-[N-3,4-(Dimethoxyphenethyl)imino]-5,6-dimethoxyindane (34)——A solution of 3,4-dimethoxyphenethylamine (**32**) (1.9 g, 11 mmole) and 5,6-dimethoxyindanone (**33**)[9] (1.9 g, 11 mmole) in dry toluene (30 ml) was refluxed in the presence of a catalytic amount of *p*-toluenesulfonic acid for 5 hr. After cooling, the separated solid was collected by filtration and recrystallized from ether to give the Schiff base (**34**) (2.2 g, 79%) as colorless prisms, mp 121—122°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1640 (>C=N–), NMR ($CDCl_3$) ppm: 2.31—2.69 (2H, m, C_2–H), 2.72—3.22 (4H, m, $2\times CH_2$), 3.34—3.95 (2H, m, $CH_2C\underline{H}_2N$=), 3.76 (3H, s, OMe), 3.79 (3H, s, OMe), 3.86 (3H, s, OMe), 3.89 (3H, s, OMe), 6.74 (4H, m, ArH) and 7.31 (1H, s, C_7–H). *Anal.* Calcd. for $C_{21}H_{25}O_4N$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.93; H, 6.98; N, 3.81.

1-[N-(3,4-Dimethoxyphenethyl)amino]-5,6-dimethoxyindane (35)——To a solution of the above Schiff base (**34**) (2.0 g, 5.6 mmole) in methanol (30 ml) was added in small portions sodium borohydride (500 mg) with stirring at 0° and the resulting mixture was stirred for 1 hr at room temperature. After evaporation

9) J. Koo, *J. Am. Chem. Soc.*, **75**, 1891 (1953).

of the solvent *in vacuo*, the residue was extracted with chloroform, and the extract was washed with water and dried over K_2CO_3. Removal of the solvent by distillation *in vacuo* gave the amine (**35**) (1.9 g, 94%) as colorless prisms, mp 87—88°, from ether. NMR ($CDCl_3$) ppm: 2.14—3.08 (8H, m, $4\times CH_2$), 3.82 (12H, s, $4\times$OMe), 4.21 (1H, m, C_1–H), and 6.64—6.86 (5H, m, ArH). *Anal.* Calcd. for $C_{21}H_{27}O_4N$: C, 70.56; H, 7.61; N, 3.92. Found: C, 70.31; H, 7.72; N, 3.88.

1-[N-(3,4-Dimethoxyphenethyl)-N-methylamino]-5,6-dimethoxyindane (**25**)——a) N-Methylation of **35**: A mixture of the above amine (**35**) (1.5 g, 4.2 mmole), 37% formalin (1 ml) and methanol (20 ml) was stirred for 1 hr at room temperature and to this solution was added sodium borohydride (500 mg) with stirring at 0°. Stirring was continued for further 1 hr at room temperature and then the solvent was distilled off *in vacuo*. The residue was extracted with chloroform and the extract was washed with water, dried over K_2CO_3 and evaporated *in vacuo* to give the 1-(N-methylamino)indane (**25**) as colorless needles, mp 91—92°, from methanol. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2795 (NMe), NMR ($CDCl_3$) ppm: 1.81—2.28 (2H, m, C_2–H), 2.26 (3H, s, NMe), 2.41—3.06 (6H, m, $3\times CH_2$), 3.78 (12H, s, $4\times$OMe), 4.39 (1H, m, C_1–H) and 6.58—6.85 (5H, m, ArH). *Anal.* Calcd. for $C_{22}H_{29}O_4N$: C, 71.13; H, 7.89; N, 3.77. Found: C, 70.94; H, 7.91; N, 3.75.

b) A Conversion from the Abnormal Reaction Product: An excess of diazomethane in ether was added to the monophenolic indane (**24**) (700 mg, 1.4 mmole) in methanol (5 ml) and the mixture was allowed to stand for 3 hr at room temperature. Evaporation of the solvent *in vacuo* afforded the nonphenolic indane (**26**) as a pale yellow syrup. NMR ($CDCl_3$) ppm: 1.88—2.34 (2H, m, C_2–H), 2.24 (3H, s, NMe), 2.42—3.07 (6H, m, $3\times CH_2$), 3.80 (6H, s, $2\times$OMe), 4.35 (1H, m, C_1–H), 5.03 (4H, s, $2\times OC\underline{H}_2Ph$), 6.48—6.91 (5H, m, ArH) and 7.18—7.54 (10H, m, $2\times OCH_2C_6\underline{H}_5$).

A mixture of this nonphenolic indane (**26**) (600 mg, 1.1 mmole) and 10% palladium on charcoal (200 mg) in methanol (30 ml) was shaken under a current of hydrogen at room temperature and at atmospheric pressure. After filtration of catalyst, the filtrate was concentrated to leave a residue, which was extracted with chloroform. The extract was washed with 10% ammonia and saturated ammonium chloride solution, dried over Na_2SO_4 and evaporated *in vacuo* to give the diphenolic indane (**27**) (250 mg) as a yellow syrup. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (–OH), NMR ($CDCl_3$) ppm: 1.85—2.42 (2H, m, C_2–H), 2.29 (3H, s, NMe), 2.52—3.12 (6H, m, $3\times CH_2$), 3.81 (6H, s, $2\times$OMe), 4.46 (1H, m, C_1–H) and 6.48—6.92 (5H, m, ArH).

To a solution of the diphenolic indane (**27**) (250 mg, 0.7 mmole) in methanol (3 ml) was added an excess of diazomethane in ether and the mixture was allowed to stand at room temperature overnight. Evaporation of the solvent gave the tetramethoxylated indane (**25**) (190 mg), colorless needles, mp 91—92° (from methanol), which was identical with the above sample in mixed melting point test and IR and NMR spectral comparisons.

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