procedure described by Waud.[32]

Gastric Acid Antisecretory Activity. Compounds were evaluated in anesthetized rats with the lumen perfused stomach preparation[33,14] and for some detailed studies in dogs equipped with well-established Heidenhain pouches. Secretion was elicited in male rats (Sprague–Dawley; Charles River, 250 g) anesthetized with urethane (1 g/kg), by constant intravenous infusion of histamine [1 mg/(kg h)]. As the stimulated acid secretion reached a steady output, compounds were injected intravenously in a series of increasing doses until the secretion was maximally suppressed. ED_{50} values were calculated from the regression lines representing percent inhibition of acid output. Histamine [60 μg/(kg h)] was also employed to stimulate acid secretion in conscious dogs. Compounds were administered by bolus intravenous injection when the stimulated acid output had stabilized. Secretion was followed by draining the pouch content at 15-min intervals and following the return of acid output to predrug levels. The dose of each compound inhibiting secretion by 50% (ED_{50}) was calculated from the regression line representing percent inhibition.

Selectivity Studies. Receptor selectivity was assessed by "in vitro" experiments on guinea pig ileum in which contractions were elicited by histamine (H_1 receptors), acetylcholine (muscarinic),

nicotine (nicotinic), or 5-hydroxytryptamine (5-HT receptors). Interference with β-adrenoceptors was evaluated in the isolated guinea pig atrium stimulated by isoproterenol.

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6-Hydroxy-4-[2-(di-*n*-propylamino)ethyl]indole: Synthesis and Dopaminergic Actions

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The title compound was proposed to be a biologically active metabolite of a dopaminergic agent, 4-[2-(di-*n*-propylamino)ethyl]indole. This proposed metabolite was synthesized by a multistep sequence beginning with methyl 3,5-dinitro o-toluate, and involving the Batcho–Leimgruber modification of the Reissert indole synthesis. The target compound exhibited high potency/activity in vivo in a cat cardioaccelerator nerve assay and in vitro in an isolated cat atrium assay. It manifested maximal pharmacological effect less than 5 min after intravenous administration in cats, as compared with a 20-min lag time following intravenous administration of the nonoxygenated congener. These pharmacological data are consistent with the proposal that the target compound is a metabolite of 4-[2-(di-*n*-propylamino)ethyl]indole.

Prior communications[1–3] have described prominent dopaminergic agonist actions of a simple indole derivative, 1, designed as a fragment of the dopaminergic ergoline
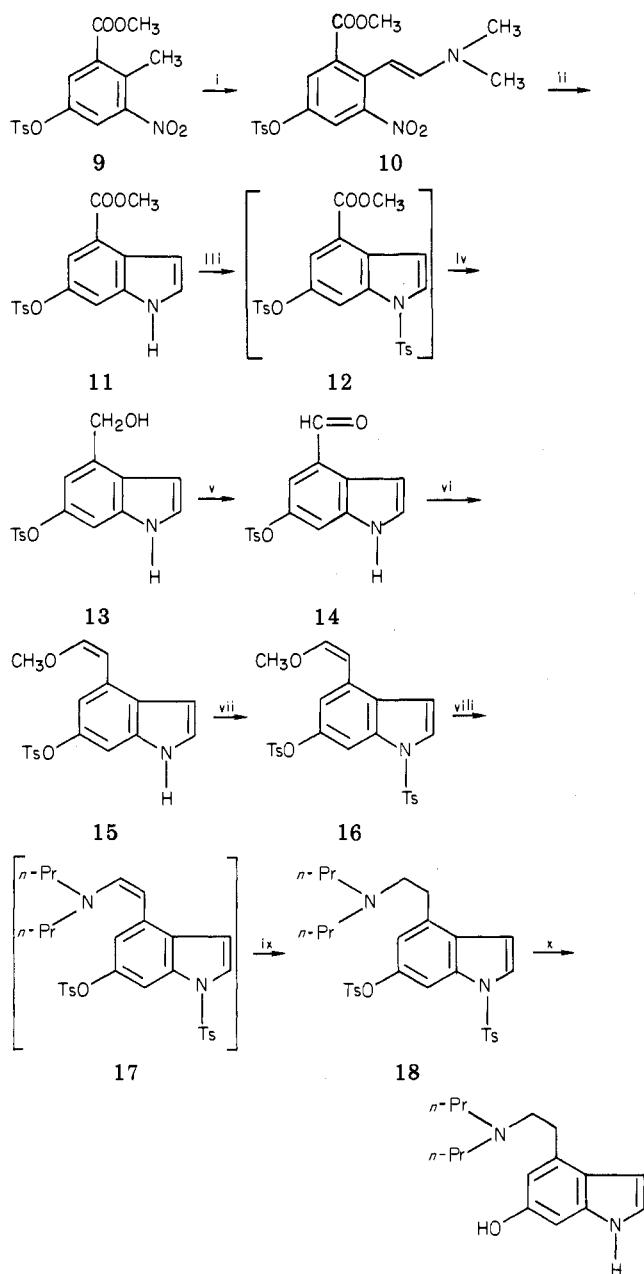

1, R = H
4, R = OH

2, R = H
3, R = OH
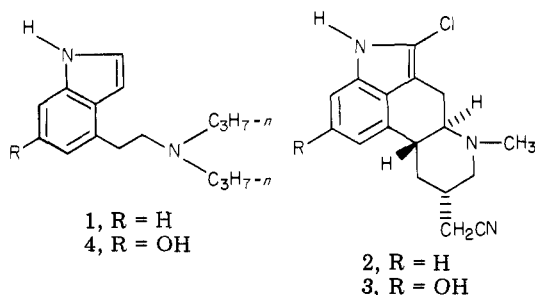
derivative lergotrile (2). The slow (30–40 min) onset of pharmacological effects following intravenous administration of 1 in intact animals, coupled with its dopaminergic inactivity in an in vitro assay using isolated cat atrium and its very weak binding activity in calf caudate tissue,[2] led to the proposal that 1 may be metabolically activated in vivo. Wong and Bymaster[4] reported that

13-hydroxylergotrile (3), a metabolite of lergotrile, had greater affinity than lergotrile in a dopamine agonist receptor binding assay. Parli et al.[5] reported that 13-hydroxylergotrile is 100 times more active than lergotrile in vitro in inhibiting prolactin release from the anterior pituitary. In the present work, it was speculated that the indole system 1 might be metabolically hydroxylated in a position and analogous to that of the 13-position of lergotrile, namely, the 6-position (structure 4). In support of this speculation are reports that rabbit liver microsomes hydroxylate tryptamine, indole-3-acetic acid, and related indoles in the 6-position[6] and that tryptamine and in-

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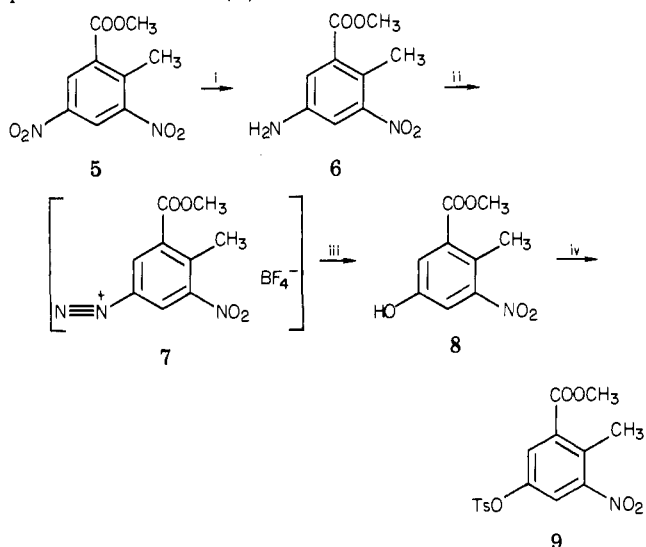
† College of Pharmacy.

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Scheme I. Preparation of
6-Hydroxy-4-[2-(di-n-propylamino)ethyl]indole (4)[a]

Scheme II. Preparation of
3-Nitro-4-methyl-5-carbomethoxyphenyl
p-Toluenesulfonate (9)[a]

[a] i = $Et_3NH^+HCOO^-$, Pd/C; ii = t-BuONO/HBF$_4$;
iii = $Cu_2O/Cu(NO_3)_2/H_2SO_4$; iv = $TsCl/K_2CO_3$.

[a] i = N,N-dimethylformamide dimethyl acetal; ii = H_2,
Pd/C; iii = TsCl; iv = LiAlH$_4$; v = MnO$_2$; vi =
$(C_6H_5)_3PCH^+OCH_3$; vii = TsCl; viii = $(n$-Pr)$_2$NH/
Hg(OAc)$_2$; ix = NaCNBH$_3$; x = n-BuLi.

mate–Pd/C system effects a partial reduction of dinitro
aromatic compounds, and the reagent system selectively
reduces the less hindered nitro group in 2,4-dinitrotoluene
to give 2-nitro-4-aminotoluene. Treatment of methyl 2-
methyl-3,5-dinitrobenzoate (5, Scheme II) with triethyl-
ammonium formate–Pd/C provided the desired 5-amino
product 6. This was converted into the starting material
9 for the Reissert indole synthesis by conventional steps
(Scheme II). The conversion of the reduction product 9
into an indole system (9 → 10 → 11, Scheme I) confirms
the selectivity of nitro group reduction in 5 (Scheme II).

The Wittig reaction on an indole-4-aldehyde to form a
(*Z*)-enol ether was described by Kozikowski et al.,[10] and
the reaction succeeded in the present work (14 → 15,
Scheme I).

Watanabe and Conlon[11] described the preparation of
vinyl ethers by vinyl transetherification of alcohols in the
presence of mercuric acetate, and Watanabe[12] described
mercuric ion catalyzed reactions of vinyl ethers with amino
alcohols to form 2-methyloxazolidines or 2-methyloxazines,
as well as reactions of vinyl ethers with 1,2-diamines to
form 2-methylimidazolidines. In the present work, it was
speculated that a simple aliphatic amine might participate
in a similar transvinylation. Indeed, treatment of the vinyl
ether 16 with di-*n*-propylamine gave the enamine 17. This
product resisted all efforts to obtain it analytically pure,
and it was used in the next step without purification. Its
reduction to the tertiary amine 18 supports the chemical
nature of 17.

Removal of the *N*-tosyl group of 18 could be achieved
with a variety of mild hydrolytic methods. However, acidic
and basic reagents and conditions sufficiently rigorous to
cleave the *O*-tosyl moiety also effected extensive decom-
position of the indole molecule. The tosyl ester group of
18 was successfully cleaved with *n*-butyllithium, in accord
with the finding[13] that aryl methanesulfonates can be

dole-3-acetic acid are hydroxylated at position 6 in the
intact rabbit.[7] Accordingly, the synthesis of 4 was un-
dertaken.

Chemistry. As shown in Scheme I, application of the
Batcho–Leimgruber modification[8] of the Reissert indole
synthesis (9 → 10 → 11) requires an *o*-nitrotoluene de-
rivative, 10, bearing an oxygen function at position 4 and
a functionality (in this case, carbomethoxy) at position 6,
capable of being homologated to an aminoethyl moiety.
Terpko and Heck[9] found that a triethylammonium for-

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(8) Batcho, A. D.; Leimgruber, W. German Patent 2 057 840, 1971; *Chem. Abstr.* **1971**, *75*, 63605v.

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cleaved to a phenol with phenyllithium.

Spectral (IR and NMR) data on all intermediates and final compounds were consistent with the proposed structures.

Pharmacological Results and Discussion

With cat in vivo experiments, the ergoline fragments 1 and 4 were active agents for inhibiting the cardioaccelerator nerve (Table I). Compound 1 was slow in onset of action, and it produced maximal inhibition approximately 20 min following intravenous administration. The time course and potency were similar to those of lergotrile (2). Compound 4 produced maximal inhibition in less than 5 min following intravenous administration, and it was significantly more active than 1. Haloperidol (100 μg/kg) or sulpiride [20 μg/(kg min)] were effective antagonists of the compounds.

When field stimulation of isolated cat atria was used to activate the sympathetic nerve terminal, compounds 1 and 4 produced very different responses. Compound 4 was a potent inhibitor of tachycardia induced by field stimulation (Table I). No alteration in resting heart rate or force of contraction was observed. Compound 1 in a concentration of 10 μM did not inhibit tachycardia induced by field stimulation, but it produced significant antagonism of the inhibition induced by apomorphine.

Compound 4 may be an active metabolite of compound 1. This is suggested by the more rapid onset of action and by the comparison of in vivo potencies of the two compounds. Also, compound 4 is a potent dopamine receptor agonist in isolated cat atrial preparations, while 1 is inactive as an agonist, being rather a weak antagonist.

Experimental Section

Melting points were determined in open glass capillaries with a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Where analyses are indicated by the symbols of the elements, analytical results were within ±0.4% of the theoretical values. IR spectra were recorded on Perkin-Elmer 267 and Beckman 4240 spectrometers. NMR spectra were recorded on a Varian Associates EM360A spectrometer with tetramethylsilane as the internal standard.

Pharmacology. Methods. In Vivo Cardioaccelerator Nerve Preparations. Cats of either sex (2–4 kg) were anesthetized with intraperitoneal injections of pentobarbital sodium (30 mg/kg). Each animal underwent a tracheotomy and was artificially ventilated with a Harvard respirator. Arterial pressure was measured from the femoral artery with a Statham P23AA transducer and a Beckmann 9857B cardiotachometer connected to a Beckmann R-611 recorder. Animals were vagotomized bilaterally, and atropine was administered (200 μg/kg iv). A midline thoractomy was performed, and the right cardioaccelerator nerve was isolated distal to the stellate ganglion. A bipolar platinum electrode was placed on the nerve and was used for electrical stimulation. The nerve was stimulated for 20 s with square wave pulses of 20 V, 2 Hz, and 5-ms duration, with a Grass 548 stimulator. A period of 5 min was allowed to elapse between electrical stimulations of the nerve. Cumulative doses of the compounds were administered intravenously at 30-min intervals. Nerve stimulation was performed every 5 min.

Isolated Atria. Cats of either sex were anesthetized as previously described. Each animal underwent a tracheotomy and was artificially ventilated with a Harvard Respirator. A midline thoractomy was performed, and a ligature was tied to the apex of the right atrium. The heart was quickly excised and placed in oxygenated Feigen solution (mM): NaCl, 154.0; KCl, 5.6; NaHCO$_3$, 23.8; glucose, 11.1; and CaCl$_2$·2H$_2$O, 5.6, dissolved in glass-distilled H$_2$O. The right atrium was dissected free of ventricular muscle, connective tissue, fat, left atrium, and blood vessels and was suspended between two platinum electrodes in a 75-mL bath containing Feigen solution. The tissue bath was maintained at 36 °C and aerated with 95% O$_2$–5% CO$_2$. The right atrium

was attached by a ligature to a Gould force transducer. Atrial rate was measured with a Beckmann cardiotachometer and a Beckmann recorder. Resting tension was adjusted to 1 g, and the preparation was allowed to equilibrate for 30 min, with the Feigen solution being changed repeatedly. The right atrium was then field stimulated with 5-ms square waves at 100 V for 10 s with a Grass stimulator. Stimulations were performed at 2, 5, and 10 Hz.

Methyl 3-Nitro-5-amino-*o*-toluate (6). To an ice-cooled solution of 58 g (0.575 mol) of Et$_3$N in 70 mL of MeCN was added over several minutes 28.4 g (0.55 mol) of 89% formic acid in 70 mL of MeCN. The resulting mixture was combined with 1.83 g of 5% Pd/C and 40 g (0.1666 mol) of methyl 3,5-dinitro *o*-toluate.[14] Moderate evolution of gas began immediately, and the reaction mixture was warmed gently to maintain gas evolution. The reaction was complete by the time the temperature of the reaction mixture reached 70 °C. The cooled reaction mixture was filtered, and the filtrate was evaporated under reduced pressure to afford a gummy residue, which was partitioned between Et$_2$O and H$_2$O. The ethereal layer was washed twice with H$_2$O, and the Et$_2$O was removed under reduced pressure to leave an orange-brown solid. This was triturated with CHCl$_3$, and the mixture was filtered. Volatiles were removed from the filtrate to provide a solid, which was recrystallized from benzene–hexane to yield 21.5 g (60%) of a bright yellow solid: mp 133–135 °C; NMR (CDCl$_3$) δ 2.48 (s, 3 H, Ar CH$_3$), 3.95 (s, 5 H, OCH$_3$, NH$_2$), 7.20 (d, 1 H, J = 1 Hz, Ar H), 7.35 (d, 1 H, J = 1 Hz, Ar H). TLC analysis (SiO$_2$, 95% CHCl$_3$, 5% EtOAc) indicated that this material was homogeneous: MS, m/e 210 (M$^+$). Anal. (C$_9$H$_{10}$N$_2$O$_4$) C, H, N.

Methyl 3-Nitro-5-hydroxy-*o*-toluate (8). To a solution of 4.2 g (0.02 mol) of 6 in 100 mL of EtOH was added 14.7 g (0.08 mol) of 48% HBF$_4$. This mixture was cooled below 0 °C, and 4.12 g (0.04 mol) of *tert*-butyl nitrite was added dropwise with stirring over a few minutes. Stirring was continued for 0.5 h, and then Et$_2$O was added in small portions over 0.5 h until no more solid separated. The solid was collected on a filter and washed with Et$_2$O to yield 4.33 g (70%) of 3-carbomethoxy-4-methyl-5-nitrobenzenediazonium fluoborate (7) as a light yellow-orange solid, mp 169–170 °C dec. This material was used in the next step without purification.

Compound 7 (4.1 g, 0.013 mol) was added in one portion to a rapidly stirred mixture of 100 g of Cu(NO$_3$)$_2$·3H$_2$O and 2.0 g of Cu$_2$O in 110 mL of 0.1 N H$_2$SO$_4$, according to a procedure of Lewin and Cohen.[15] After 15 min, the aqueous phase was decanted from the gummy material that separated. A fresh 2.0-g portion of Cu$_2$O was added to the aqueous phase, and a second 4.1-g (0.013 mol) portion of 7 was added. After 15 min, the gummy material that again formed was separated, and the aqueous phase was combined with of third 2.0-g portion of Cu$_2$O and a third 4.1-g portion of 7 [total amount of 7 employed, 12.3 g (0.04 mol)]. The combined gummy products were taken up in CHCl$_3$, and the resulting solution was filtered. Evaporation of the filtrate left a dark oil, which was taken up in Et$_2$O. The ethereal solution was filtered, and the filtrate was evaporated to leave a dark gum, which was chromatographed on SiO$_2$ and eluted with CHCl$_3$ to give 2.7 g (32%) of a light yellow solid, which was recrystallized from benzene: mp 114–115 °C; MS, m/E 211 (M$^+$). Anal. (C$_9$H$_9$NO$_5$) C, H, N.

3-Nitro-4-methyl-5-carbomethoxyphenyl *p*-Toluenesulfonate (9). A mixture of 9.0 g (0.043 mol) of 8, 8.12 g (0.043 mol) of *p*-toluenesulfonyl chloride, and 7.18 g (0.05 mol) of K$_2$CO$_3$ in 75 mL of Me$_2$CO was stirred at room temperature for 3.5 h. The mixture was then filtered, and the dried (Na$_2$SO$_4$) filtrate was evaporated under reduced pressure to leave a thick orange oil, which solidified on standing and was recrystallized from MeOH to afford 14.9 g (95%) of product: mp 83–84 °C; MS, m/e 365 (M$^+$). Anal. (C$_{16}$H$_{15}$NO$_7$S) C, H, N.

3-Nitro-4-[2-(dimethylamino)ethenyl]-5-carbomethoxyphenyl *p*-Toluenesulfonate (10). Compound 9 (5 g, 0.014 mol) and 5 mL (ca. 0.042 mol) of *N,N*-dimethylformamide dimethyl acetal were heated in 7.5 mL of DMF under N$_2$ at 115 °C for 40

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(15) Lewin, A. H.; Cohen, T. *J. Org. Chem.* 1967, *32*, 3844.

Table I. Sympathetic Neuronal Activity of Lergotrile (1), 4-[2-(Di-*n*-propylamino)ethyl]indole (2), and Its 6-Hydroxy Analogue 4

no.	in vivo cat cardioaccelerator nerve: ED_{50} (95% CL), μmol/kg iv	in vitro cat atria: ED_{50}, μM
1	0.22 (0.12–0.33)	inactive[a]
2	0.27 (0.13–0.62)	b
4	0.019 (0.013–0.026)	0.027 (0.019–0.044)
4	0.047 (0.032–0.069)[c]	

[a] Compound 1 showed no inhibition with concentrations up to 10 μM. This concentration significantly antagonized the inhibitory action of apomorphine. [b] Not tested. [c] ED_{50} values following intraduodenal administration of 4.

min. Volatiles were then evaporated under reduced pressure to leave a dark red oil, which was diluted with 40 mL of toluene. The toluene mixture was filtered, and the filtrate was evaporated under reduced pressure. The dark residue was triturated with MeOH to afford 3.5 g (61%) of a red-orange solid: mp 131–132 °C; MS *m/e* 420 (M⁺). Anal. ($C_{19}H_{20}N_2O_7S$) C, H, N.

4-Carbomethoxy-6-(*p*-toluenesulfonyloxy)indole (11). Compound 10 (0.84 g, 0.002 mol) was hydrogenated over 0.17 g of 5% Pd/C in 20 mL of benzene at an intial pressure of 25 psig, until the dark red color disappeared (ca. 3 h). The clear orange mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was chromatographed on SiO_2 and eluted with $CHCl_3$ to afford 0.345 g (50%) of solid product: mp 127–128 °C (benzene–hexane); MS, *m/e* 345 (M⁺). Anal. ($C_{17}H_{15}NO_5S$) C, H, N.

4-(Hydroxymethyl)-6-(*p*-toluenesulfonyloxy)indole (13). Compound 11 (0.345 g, 0.001 mol), 0.191 g (0.001 mol) of *p*-toluenesulfonyl chloride, and 0.276 g (0.002 mol) of K_2CO_3 in 4 mL of Me_2CO were stirred at room temperature for 4 h. The reaction mixture was filtered, and the solids on the filter were washed twice with benzene. The organic solutions were pooled, and volatiles were removed under reduced pressure to leave 1-*p*-toluenesulfonyl-4-carbomethoxy-6-(*p*-toluenesulfonyloxy)indole (12) as an orange brown oil. NMR ($CDCl_3$) δ 2.46 (s, 6 H, Ar CH_3), 3.93 (s, 3 H, OCH_3), 6.8–8.0 (m, 12 H, Ar H). This material was unstable, and it resisted all attempts to purify it. It was used in the next step without purification.

Crude 12, prepared from 7.0 g (0.02 mol) of 11, in 70 mL of THF at 0 °C was treated with 0.9 g (0.024 mol) of $LiAlH_4$, added in small increments. When TLC analysis (SiO_2, 5% EtOAc in $CHCl_3$) showed that the reduction was complete, excess saturated Na_2SO_4 was added, and the resulting mixture was filtered. The filter cake was washed with $CHCl_3$. The combined filtrates were evaporated, and the dark brown oily residue (ca. 6 g) was chromatographed on 90 g of SiO_2 and eluted with $CHCl_3$. The major fraction yielded a light brown solid, which was recrystallized from benzene to afford 2.3 g (36% from 11) of white crystals: mp 102–103 °C; MS, *m/e* 317. Anal. ($C_{16}H_{15}NO_4S$) C, H, N.

4-Formyl-6-(*p*-toluenesulfonyloxy)indole (14). To a stirred solution of 1.03 g (0.003 mol) of 13 in 20 mL of CH_2Cl_2 was added 3.0 g of MnO_2 (85%) in small portions over 2 h, until TLC analysis (SiO_2, $CHCl_3$) indicated the presence of no more starting material. The resulting mixture was filtered, and the filtrate was evaporated. The orange solid residue was triturated with CH_2Cl_2–hexane to give 0.86 g (84%) of a pale yellow powder: mp 174–176 °C (benzene–hexane); MS, *m/e* 315 (M⁺). Anal. ($C_{16}H_{13}NO_4S$) C, H, N.

(*Z*)-4-(2-Methoxyvinyl)-6-(*p*-toluenesulfonyloxy)indole (15). To an ice-cooled mixture of 1.29 g (0.00375 mol) of (methoxymethyl)triphenylphosphonium chloride in 4 mL of dry THF was added 2.4 mL of 1.64 M *n*-BuLi in hexane (0.00394 mol). After 0.5 h at room temperature, 0.47 g (0.0015 mol) of 14 was added in one portion. This mixture was stirred at room temperature for 0.75 h and then treated with 10 mL of H_2O, and the resulting mixture was extracted with benzene. The benzene extract was dried (Na_2SO_4) and evaporated, and the residue was chromatographed on SiO_2 and eluted with 1:1 CH_2Cl_2–hexane to

yield 0.33 g (64%) of solid material: mp 164–165 °C (from benzene); MS, *m/e* 343 (M⁺). Anal. ($C_{18}H_{17}NO_4S$) C, H, N.

(*Z*)-1-*p*-Toluenesulfonyl-4-(2-methoxyvinyl)-6-(*p*-toluenesulfonyloxy)indole (16). To a stirred mixture of 0.17 g (0.0005 mol) of 15, 0.075 g (0.002 mol) of powdered NaOH, and 0.015 g of tetra-*n*-butylammonium bisulfate in 2 mL of CH_2Cl_2 was added 0.30 g (0.0015 mol) of *p*-toluenesulfonyl chloride in small portions over 1 h. The reaction mixture was filtered, and the filtrate was evaporated under reduced pressure to afford an oil, which decomposed on standing for a few hours and was used immediately in the next step without purification: MS, *m/e* 498 (M + 1) (CI, NH_3); NMR ($CDCl_3$) δ 2.35 (s, 3 H, Ar CH_3), 2.46 (s, 3 H, Ar CH_3), 3.73 (s, 3 H, OCH_3), 5.40 (d, 1 H, =CH, J = 7 Hz), 6.25 (d, 1 H, =CH, J = 7 Hz), 6.65–8.00 (m, 12 H, Ar H).

1-*p*-Toluenesulfonyl-4-[2-(di-*n*-propylamino)ethyl]-6-(*p*-toluenesulfonyloxy)indole (18). A mixture of 0.5 g (0.001 mol) of 16, 7 mL of di-*n*-propylamine, 0.05 g of $Hg(OAc)_2$, and 2.5 mL of benzene was warmed at 45 °C for 5 h. The reaction mixture was diluted with 20 mL of benzene, and this solution was washed with H_2O and dried (Na_2SO_4). Evaporation of the volatiles gave 1-*p*-toluenesulfonyl-4-[2-(di-*n*-propylamino)vinyl]-6-(*p*-toluenesulfonyloxy)indole (17) as an oil, which was used in the next step without purification: NMR ($CDCl_3$) δ 0.90 (t, 6 H, CH_3), 1.53 (quintet, 4 H, NCH_2CH_2), 2.34 (s, 3 H, Ar CH_3), 2.47 (s, 3 H, Ar CH_3), 3.10 (t, 4 H, NCH_2), 5.0–5.8 (m, 2 H, HC=CH), 6.6–8.0 (m, 12 H, Ar H).

Compound 17 (0.9 g, 0.0016 mol) in 20 mL of MeCN was treated with 0.2 g (0.003 mol) of $NaCNBH_3$, added in one portion. AcOH was added dropwise from time to time to maintain the pH near 7 (pH paper). After 10 min, TLC analysis (SiO_2; EtOAc–$CHCl_3$, 1:20) showed almost complete absence of starting material. The reaction mixture was then partitioned between equal convenient volumes of H_2O and benzene. The benzene layer was shaken with saturated $NaHCO_3$, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on 20 g of SiO_2 and eluted with $CHCl_3$ to give 0.7 g (78%) of a yellow oil: NMR ($CDCl_3$) δ 0.83 (t, 6 H, CH_3), 1.42 (m, 4 H, NCH_2CH_2), 2.36 (s, 3 H, ArCH_3), 2.46 (s, 3 H, Ar CH_3), 2.60 (m, 8 H, NCH_2, Ar CH_2), 6.70 (m, 2 H, Ar H), 7.1–7.9 (m, 10 H, Ar H); MS, no parent peak. The highest mass peak was *m/e* 229 (M⁺ – 2Ts – C_2H_5). An analytical sample was purified by preparative TLC (SiO_2, EtOAc). Anal. ($C_{30}H_{36}N_2O_5S_2$) C, H, N.

4-[2-(Di-*n*-Propylamino)ethyl]-6-hydroxyindole Acetate (4). To 0.7 g (0.0013 mol) of 18 in 25 mL of benzene at 10 °C was added rapidly 14 mL of a 1.6 M solution of *n*-BuLi in hexane (0.0224 mol). After this addition, the reaction vessel was removed from the cooling bath, and the mixture was stirred for 4 min. It was then immediately placed in an ice bath and treated with 2 mL of AcOH, added in one portion. A colorless solid separated from the exothermic reaction mixture. This mixture was diluted with 30 mL of benzene, and an additional 2-mL portion of AcOH was added. The resulting mixture was filtered, and the filter cake was washed thoroughly with benzene. The combined filtrates were concentrated at the top of a silica column (8 g), by allowing the benzene solution to flow through rapidly, and then the column was eluted with EtOAc. The eluate was evaporated under reduced pressure, and the residue was recrystalllized from EtOAc to provide 0.216 g (54%) of light green crystals: mp 154–157° C; MS, *m/e* 260 (M⁺ – AcOH); NMR ($CDCl_3$) δ 0.95 (t, 6 H, CH_3), 1.68 (m, 4 H, CH_2CH_3), 1.97 (s, 3 H, CH_3COO^-), 2.85–3.23 (m, 8H, CH_2), 6.43 (d, H(3), J = 3 Hz), 6.57 (d, 1 H, Ar H, J = 2 Hz), 6.80 (d, 1 H, Ar H, J = 2 Hz), 7.15 (d, H(2), J = 3 Hz). Anal. ($C_{18}H_{28}N_2O_3$) C, H, N.