mp 195–198 °C dec; $[\alpha]^{17}_D$ −34° (c 0.25, ethanol); R_f 0.29 (C); IR (KBr) 3100 (s, OH, NH_2), 1710 (s, adenine), 1600 cm^{-1} (m, adenine); NMR [$(CD_3)_2SO$–D_2O, 9:1] δ 1.0–1.4 (9 H, m, H-6–H-9), 1.25 (3 H, d, $J_{1,2}$ = 6.3, H-1), 1.95–2.05, 2.3–2.45 (4 H, m, H-4, H-5), 4.48 (1 H, dt, $J_{2,3}$ = 3.5, H-2), 4.78–4.88 [1 H, m (8 lines), H-3], 8.39 (2 H, br s, NH_2), 8.65, 8.79 (2 H, 2 s, H-2, H-8).

Anal. Calcd for $C_{14}H_{23}N_5O$·2.0HCl: C, 45.90; H, 6.88; N, 19.12; Cl, 19.35. Found: C, 45.87; H, 6.89; N, 19.11; Cl, 19.28.

(2*R*,3*R*)-3-(Adenin-9-yl)-2-nonanol Dihydrochloride 15b. By the procedure of **14b**, 163 mg (0.44 mmol) of **15a** was converted to 30 mg (22%) of **15b**, isolated as the dihydrochloride; physical and spectral data were identical with those of **13b**; $[\alpha]^{20}_D$ +33.5° (c 0.25, ethanol).

Anal. Calcd for $C_{14}H_{23}N_5O$·2HCl: C, 45.90; H, 6.88; N, 19.12; Cl, 19.35. Found: C, 45.92; H, 6.89; N, 19.12; Cl, 19.31.

(2*S*)-2-(Benzyloxy)-3-nonanone (18). To a stirred solution of 5.60 g (22.5 mmol) of a mixture of (2*S*,3*R* or *S*)-2-*O*-benzyl-2,3-nonanediols (**9a** and **10a**) in 250 mL of anhydrous dichloromethane was added 7.30 g (33.7 mmol) of pyridinium chlorochromate (Aldrich) in one portion. After being stirred for 10 h at 25 °C, the mixture was poured over a 200 g column of dry silica gel, and the column was eluted with 1 L of 1:1 methanol–chloroform. The solvents were evaporated, and the resulting crude oil was distilled in vacuo to give 4.0 g (72%) of **18**: bp 125–126 °C (0.25 torr); $[\alpha]^{18}_D$ −32.0° (c 1.2, chloroform); R_f 0.56 (A); IR (film) 1730 cm^{-1} (s, C=O); NMR ($CDCl_3$) δ 0.7–1.6 (9 H, m, H-6–H-9), 1.30 (3 H, d, $J_{1,2}$ = 6.3, H-1), 3.93 (1 H, q, H-2), 4.55 (2 H, s, $PhCH_2$), 7.2–7.45 (5 H, m, Ph).

Anal. Calcd for $C_{16}H_{24}O_2$·0.6H_2O: C, 74.15; H, 9.80. Found: C, 74.12; H, 9.38.

General Procedure for the Reduction of (2*S*)-2-(Benzyloxy)-3-nonanone (18) with Various Hydride Reducing Agents. (A) Reduction. To a stirred solution of 0.03 g (0.12 mmol) of (2*S*)-2-(benzyloxy)-3-nonanone (**18**) in 2 mL of tetrahydrofuran (exception: sodium borohydride was used with absolute methanol as the solvent) maintained at the indicated temperature (see Table I for specific conditions) and under nitrogen atmosphere was added 0.12 mmol of the appropriate hydride reducing agent. After warming to room temperature, the mixture was stirred for 24 h, at the end of which time the excess hydride was decomposed by using the indicated reagent(s) (see Table I). The mixture was filtered through Celite, and the filtrate was diluted to exactly 10 mL with tetrahydrofuran.

(B) Gas–Liquid Chromatographic (GLC) Analysis. Quantitative GLC analysis of each reaction mixture was carried out by using a Research Specialties Co. Model 600 GLC apparatus, equipped with a hydrogen flame-ionization detector and a 0.3 × 185-cm glass column packed with 3.5% Emulfor on 80–120-mesh Chromosorb W (nitrogen carrier gas at ca. 20 mL min^{-1}) at a 190 °C column temperature. The percent yield and 2*S*,3*R* to 2*S*,3*S* (erythro/threo) product composition were determined by comparison of peak heights and known standards of both (2*S*,3*R*)-2-*O*-benzyl-2,3-nonanediol (**9a**) and (2*S*,3*S*)-2-*O*-benzyl-2,3-nonanediol (**10a**). Results are tabulated in Table I.

(2*S*,3*S*)-2-*O*-Benzyl-3-*O*-(+)-[α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetyl]nonanediol and (2*R*,3*R*)-2-*O*-benzyl-3-*O*-(+)-[α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetyl]nonanediol were prepared according the established procedure[16] by using 330 mg (1.0 mmol) of (+)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetic trifluoroacetic anhydride[16] and 144 mg (0.6 mmol) of (2*S*,3*S*)-2-*O*-benzyl-2,3-nonanediol (**10a**) or 61 mg (0.2 mmol) of (2*R*,3*R*)-2-*O*-benzyl-2,3-nonanediol (**12a**). The products were purified via liquid chromatography over 50 g of silica gel, eluting with 2:3 chloroform/*n*-hexane). Very viscous oils of each were obtained: R_f 0.32 (1:1 chloroform/*n*-hexane); mass spectrum, calcd for $M^+ \cdot$ *m/e* 566.2644, found *m/e* 566.2630 and 566.2632, respectively, for the derivative of **10a** and the derivative of **12a**. NMR spectra were consistent with the proposed structures.

Acknowledgment. R. B. Jarrell and R. Pajares, III, are thanked for some experimental work. This work was supported, in part, by the National Institutes of Health (Grant CA-26465) and the University of Alabama Research Grants Committee. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. The NMR spectrometer was purchased under a grant from the National Science Foundation. L.D.H. gratefully acknowledges the Graduate School of The University of Alabama for the award of a research fellowship.

Registry No. 1, 3969-60-6; 2, 81408-31-3; 3, 4697-98-7; 4, 81408-32-4; 5, 4613-16-5; 6, 81408-33-5; 7, 81445-44-5; 8, 81445-45-6; 9a, 81408-34-6; 9b, 81408-35-7; 10a, 81408-36-8; 10b, 81408-37-9; 11a, 81408-38-0; 11b, 81408-39-1; 12a, 81408-40-4; 12b, 81408-41-5; 13a, 81408-42-6; 13b·2HCl, 81408-43-7; 14a, 81408-44-8; 14b·HCl, 81408-45-9; 15a, 81408-46-0; 15b·2HCl, 81408-47-1; 16a, 81408-48-2; 16b·HCl, 81408-49-3; 17, 6748-69-2; 18, 81408-50-6; (2*S*,3*S*)-2-D-benzyl-3-*O*-(+)-[α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetyl]nonane, 81408-51-7; (+)-α-[1-(9-anthryl)-2,2,2-trifluoroethoxy]acetic trifluoroacetic anhydride, 81408-52-8.

A New Class of *D*-Heteroergolines: Total Synthesis and Resolution of a 9-Oxaergoline, 4,6,6a,8,9,10a-Hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine

Paul S. Anderson, John J. Baldwin, David E. McClure, George F. Lundell, and James H. Jones*

Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania 19486

Received January 8, 1982

Synthesis of the 9-oxaergoline ring system, 4,6,6a,8,9,10a-hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine, is presented. Both the C/D cis and the C/D trans isomers were prepared. Resolution of the C/D trans isomer afforded (−)-*trans*-6-ethyl-9-oxaergoline, **15**, which has the same configuration as the natural ergolines, namely, 6a*R*,10a*R*, and possesses potent dopamine agonist properties.

The ergot alkaloids, metabolic products of the parasitic fungus *Claviceps*, represent a widely studied structural class of compounds possessing a range of important biological properties.[1-4] The majority of the ergots contain the tetracyclic ergoline ring system, **16**.[5] The extended trans arylethylamine[6] substructure, contained within this rigid tetracyclic framework, has been viewed as the key element responsible for the interaction of these compounds

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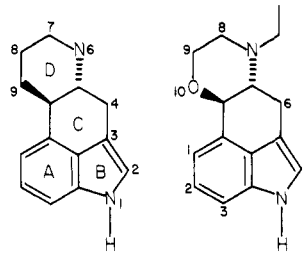


16 (−)-15

with adrenergic and dopaminergic receptors.[7]

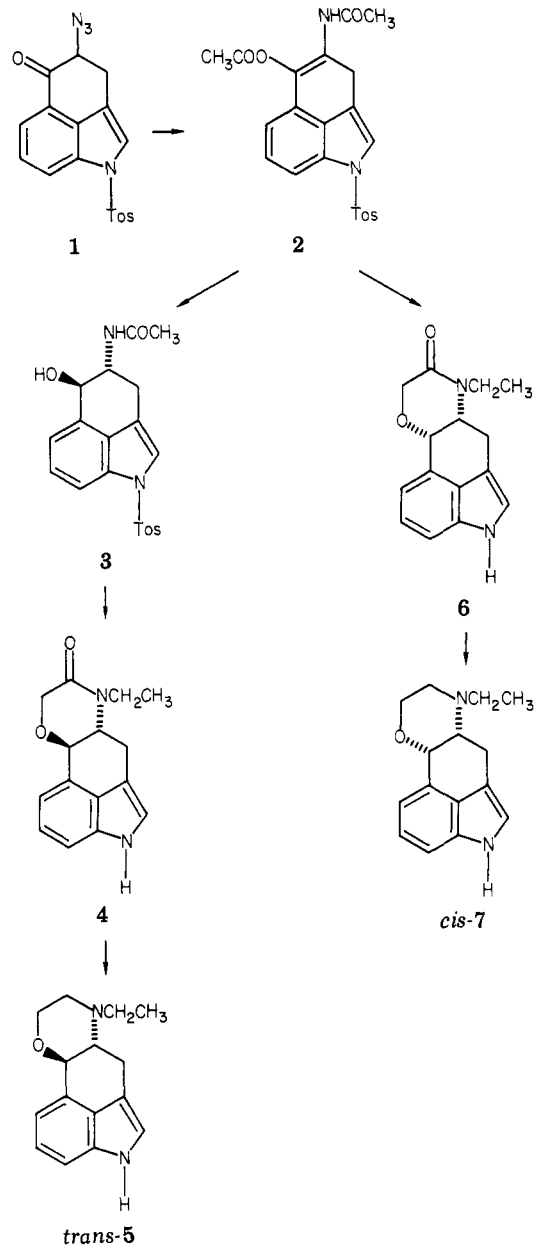
In this regard, two semisynthetic ergoline derivatives, 2-bromo-α-ergocryptine and pergolide, have been found useful in the treatment of Parkinson's disease,[8] a condition in which striatal dopamine deficiency is a generally accepted cause. In an evaluation of related ring systems containing the extended arylethylamine moiety, we have prepared both *cis*- and *trans*-4,6,6a,8,9,10a-hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine, the first examples of totally synthetic 9-oxaergolines.[9] In the design of this novel ring system, the π-electron center present in the Δ^8 and Δ^9 ergolines such as lysergic and paspalic acids has been replaced by the unoccupied p orbitals of oxygen. In addition, the individual enantiomers of the racemic trans isomer have been prepared by resolution of the acetylamine alcohol precursor followed by formation of the fused morpholine ring.

Results and Discussion

The synthetic sequence used to prepare both *cis*- and *trans*-4,6,6a,8,9,10a-hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine **5** and **7** is presented in Scheme I. The *trans*-oxaergoline, compound **5**, was obtained via the LAH reduction of the *trans*-benzoxazinone **4**. When the *trans*-acetylamino alcohol **3** was treated with an excess of LAH in THF and dimethoxyethane, deprotection of the tosyl group was accompanied by reduction of the amide to an ethylamine moiety. Without isolation, the intermediate amino alcohol was acylated with chloroacetyl chloride and cyclized with NaH to yield the desired benzoxazinone **4**. $NaBH_4$ reduction of the acetoxy intermediate **2** produced the *trans*-acetylamino alcohol **3** (J = 9 Hz; diaxial protons) as noted previously by Bowman et al.[10] The diacetate **2** was prepared by catalytic hydrogenation of azide **1**[10] in acetic anhydride and THF; acetylation occurred on the enolized ketone as well as the free amino group. When **2** was reduced with LAH followed by acylation with chloroacetyl chloride and cyclization with NaH, a two-component mixture was obtained. This mixture was cleanly separated by medium-pressure chromatography,[11] using $CHCl_3$–EtOAc (9:1) as eluant. The component with the higher R_f was identical with **4** obtained via LAH reduction of **3** (supra vida). The slower moving component, obtained in 25% yield, was the *cis*-oxazinone **6** (J = 3 Hz). It is assumed the amino group in this *cis*-oxazinone is in the preferred equatorial conformation and thus the oxygen must be axial. LAH reduction of **6** afforded the *cis*-oxazine **7**; the proton adjacent to oxygen at the ring junction of **7** appears as a broad singlet.

Within the ergoline and Δ^8 ergoline classes, the C,D ring

Scheme I



trans-5

junction is trans and has the *R,R* configuration.[12] It was, therefore, of interest to prepare the individual enantiomers of the *trans*-oxaergoline **5** for stereochemical comparison to the natural ergots. Scheme II details the synthetic method used to effect this resolution.[13] The trans alcohol **3** was esterified with the (−) isomer of *O*-methylmandelic acid to afford the diastereomeric esters **8** and **12**. The esterification required the use of 4-(dimethylamino)-pyridine as catalyst.[14] The diastereomeric esters were separated cleanly by medium-pressure chromatography,[11] using CH_2Cl_2–acetone (9:1) as the eluting solvent. The resolved esters were hydrolyzed by brief treatment with ethanolic KOH to provide the resolved alcohols **9** and **13** in excellent yield. Each resolved alcohol was carried through the remaining steps of the synthesis to provide the (+) isomer **11** and (−) isomer **15** of *trans*-9-oxaergoline **5**. The (−)-*trans*-9-oxaergoline **15** retained the potent

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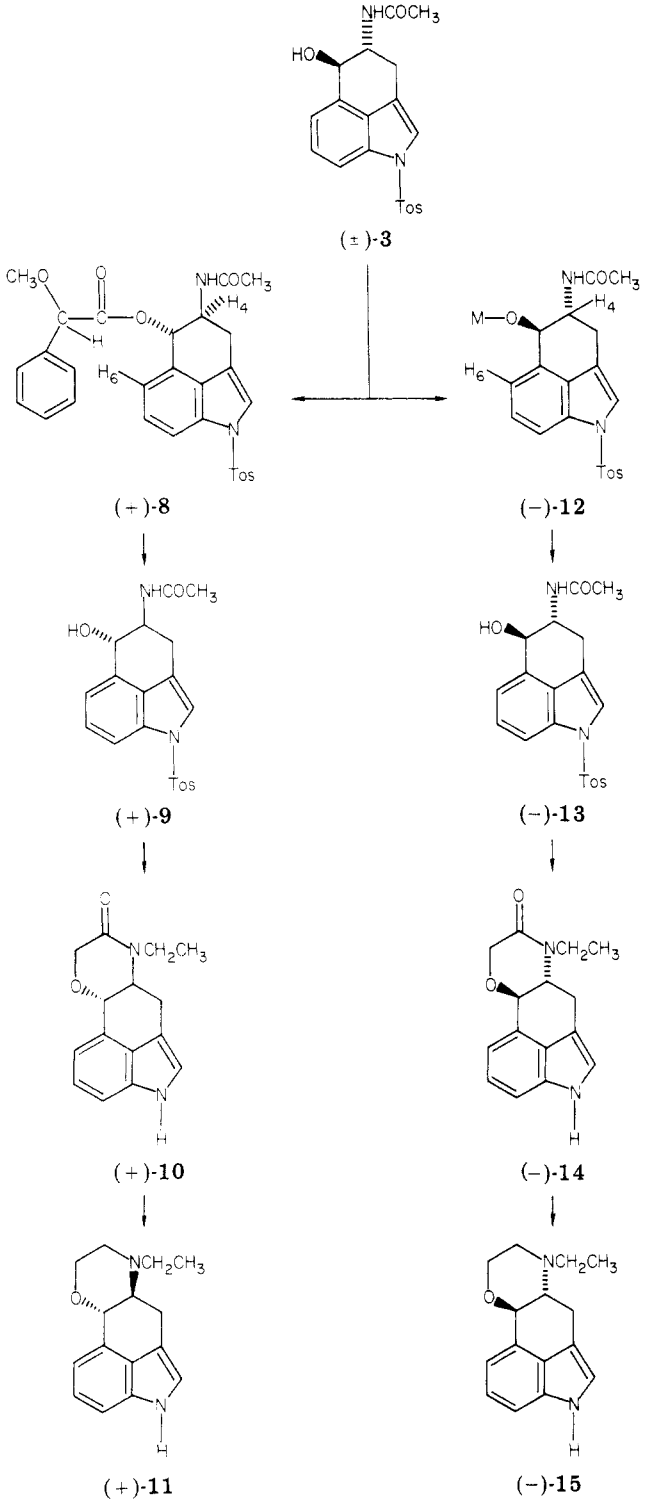
Scheme II



dopamine agonist properties,[15] while the (+) isomer showed greatly diminished activity.

Since the resolved mandelate esters were available, the rules of Moser and Dale[16] were used to predict the absolute configuration of compound **15**. The NMR data[17] suggest that the alcohol portion of ester **12** is in the *R* configuration. Since the amine and the alcohol are trans to each other in **15**, the conclusion becomes that (−)-*trans*-9-oxaergoline **15** has the *R,R* absolute configuration[18] and is identical with that of the natural ergolines.

Experimental Section

General Procedures. Melting points were determined on a Thomas-Hoover capillary melting-point apparatus and are uncorrected. The ^1H NMR spectra were taken on a Nicolet 360-MHz or a Varian T-60A spectrometer using Me_4Si as an internal standard. Optical rotations were determined with a Perkin-Elmer 141 polarimeter. Solutions were dried over Na_2SO_4 and concentrated, using a Buchi rotary evaporator under water aspirator pressure.

4-(Acetylamino)-5-acetoxy-1,3-dihydro-1-(*p*-tolylsulfonyl)benz[*cd*]indole (2). Hydrogen was bubbled into a solution of azide **1**[10] (5 g, 1.36 mmol) in THF (150 mL) and Ac_2O (50 mL), which contained 1.2 g of 10% Pd/C catalyst, at room temperature and pressure for 2 h. The reaction mixture was filtered and then evaporated to dryness in vacuo, affording a yellow solid that was washed with petroleum ether. The yield was 5.0 g (96%) of crude **2**, which contained two spots by TLC analysis [EtOAc–hexane (1:1)]; however, the material was suitable for use without further purification. Recrystallization from EtOAc gave pure **2**: mp 235–237 °C dec; NMR (Me_2SO-d_6) δ 2.1 (s, 3 H, $ArCH_3$), 2.3 (s, 3 H, $NCOCH_3$), 2.42 (s, 3 H, $OCOCH_3$), 3.34 (s, 2 H), 7.12–7.84 (8 H, ArH).

Anal. Calcd for $C_{22}H_{20}N_2O_5S$: C, 62.25; H, 4.75; N, 6.60. Found: C, 62.01; H, 4.72; N, 6.60.

***trans*-4-(Acetylamino)-1,3,4,5-tetrahydro-1-(*p*-tolylsulfonyl)benz[*cd*]indol-5-ol (3).** $NaBH_4$ (0.5 g) was added in portions to a stirred solution of **2** (4.0 g) in THF (70 mL) and EtOH (15 mL) at room temperature. Stirring was continued for 1 h and then the reaction mixture was poured into H_2O (250 mL) and acidified with dilute HCl and the precipitated product recovered by filtration to yield 3.8 g of **3** (95%), mp 155–160 °C. Recrystallization from EtOAc gave pure material: mp 168–170 °C (lit.[10] mp 123–125 °C); NMR (Me_2SO-d_6) δ 1.8 (s, 3 H, $ArCH_3$), 2.3 (s, 3 H, $NCOCH_3$), 4.68 (t, 1 H), 7.25–7.85 (8 H, ArH).

Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29. Found: C, 62.55; H, 5.59; N, 7.43.

***trans*-4,6,6a,7,9,10a-Hexahydro-7-ethylindolo[3,4-*gh*][1,4]benzoxazin-8-one (4).** To a stirred suspension of LAH (9.0 g) in THF (130 mL) cooled to 10–15 °C was added a solution of trans alcohol **3** (20 g, 5.23 mmol) in THF (150 mL) and 1,2-dimethoxyethane (100 mL). The reaction mixture was heated at reflux for 1 h and cooled to 10 °C, and 2-propanol (20 mL) was added. To the cooled mixture was added 10 mL of a saturated solution of Na_2SO_4 and 200 mL of CH_2Cl_2. This mixture was filtered through Supercel and the filter cake washed twice with 200 mL of CH_2Cl_2. The filtrate was concentrated to about 100 mL in vacuo and then diluted with EtOAc (250 mL). To the EtOAc solution was added a solution of Na_2CO_3 (38 g) in H_2O (200 mL); this mixture was stirred rapidly and 6 mL of chloroacetyl chloride added dropwise. The organic layer was separated, washed with brine, dried over Na_2SO_4, and evaporated to dryness in vacuo. The residue was dissolved in THF (30 mL) and CH_3CN (30 mL) and added to a suspension of NaH (3 g of 53% mineral oil suspension) in THF (30 mL). After 0.5 h, several milliliters of ethanol was added to destroy excess NaH and then the reaction mixture was poured into water (300 mL). Neutralization with HOAc afforded *trans*-oxazinone **4** as a solid that was filtered and dried to yield 10 g (75%), mp 275–280 °C dec. Recrystallization from EtOH afforded pure material: mp 282–284 °C dec; NMR (Me_2SO-d_6) δ 1.1 (t, 3 H, CH_2CH_3), 4.35 (d, 1 H, J = 17 Hz), 4.42 (d, 1 H, J = 17 Hz), 5.06 (d, 1 H, J = 9 Hz), 6.9–7.3 (4 H, ArH), 10.86 (br m, 1 H, NH).

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.25; H, 6.37; N, 11.07.

***trans*-4,6,6a,8,9,10a-Hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine (5).** To a stirred suspension of LAH (4.2 g) in THF (150 mL) at 10–15 °C was added a solution of *trans*-benzoxazinone **4** (10 g, 3.9 mmol) in THF (600 mL) and 1,2-dimethoxyethane (200 mL). The reaction mixture was heated at reflux for 0.5 h and then cooled to 10–15 °C. Excess LAH was destroyed by the addition of 2-propanol (17 mL) and saturated

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(17) **12** H_4 minus **8** H_4 = −0.14; **12** H_6 minus **8** H_6 = +0.08. Thus **12** is the *R,R* isomer.
(18) A single-crystal X-ray analysis is in progress.

Na_2SO_4 solution (7 mL), 200 mL of CH_2Cl_2 was added, and the mixture was filtered through Supercel. After being washed with CH_2Cl_2, the filtrate was evaporated to dryness in vacuo. The resulting white solid was washed with Et_2O. The crude yield of **5** was 5.8 g (62%), mp 210–215 °C dec. The pure product was crystallized from THF: mp 217–219 °C dec; NMR (Me_2SO-d_6) δ 1.06 (t, 3 H, CH_2CH_3), 4.57 (d, 1 H, J = 9 Hz), 6.9–7.3 (4 H, ArH), 9.55 (br m, 1 H, NH).

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.48; N, 11.55. Found: C, 74.40; H, 7.55; N, 11.41.

***cis*-4,6,6a,7,9,10a-Hexahydro-7-ethylindolo[3,4-*gh*][1,4]benzoxazin-8-one (6).** To a stirred suspension of LAH (7 g) in THF (200 mL), cooled to 5–10 °C, was added dropwise a solution of **2** (13 g, 3.4 mmol) in THF (200 mL) and 1,2-dimethoxyethane (200 mL). The reaction mixture was heated at reflux for 1.5 h and then cooled in an ice bath to 10 °C. 2-Propanol (20 mL) was added, followed by 10% NaOH (14 mL). The mixture was filtered through Supercel, the filter cake was washed with ethyl acetate, and the filtrate was concentrated in vacuo. The resulting red oil was partitioned between ethyl acetate (200 mL) and a citric acid solution (12 g in 100 mL of H_2O). The acid layer was separated, layered with ethyl acetate (200 mL), and then made basic by the addition of solid Na_2CO_3 (25-g portion). To this mixture was added chloroacetyl chloride (2.5 mL). The organic phase was separated, washed with brine, dried, and then evaporated in vacuo. The residue was taken up in THF (50 mL) and CH_3CN (50 mL) and added to a stirred suspension of NaH (2.5 g of 53% mineral oil suspension) in THF (50 mL). After 1 h, the reaction was poured into H_2O (500 mL), acidified with HOAc, and extracted with EtOAc (2 × 200 mL). The dried EtOAc extracts contained two major spots by TLC [SiO_2/$CHCl_3$–EtOAc (9:1)]. The organic layer was concentrated to a small volume and subjected to medium-pressure chromatography over silica gel, using $CHCl_3$–EtOAc (9:1) to elute. The fraction with the higher R_f proved to be identical with **4** (3.6 g, 41%). The slower moving component proved to be the cis fused derivative **6** (2.2 g, 25%, mp 220–222 °C): NMR (Me_2SO-d_6) δ 1.06 (t, 3 H, CH_2CH_3), 4.9 (d, 1 H, J = 3 Hz), 6.9–7.2 (4 H, ArH).

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.45; H, 6.57; N, 11.08.

***cis*-4,6,6a,8,9,10a-Hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine (7).** The reduction of *cis*-benzoxazinone **6** was carried out exactly as described above for the reduction of the corresponding trans isomer. The yield of **7** was 88%: mp 170–172 °C (crystallized from CH_3CN); NMR (Me_2SO-d_6) δ 1.02 (t, 3 H, CH_2CH_3), 4.62 (br s, 1 H), 6.87–7.23 (4 H, ArH), 10.7 (s, 1 H, NH).

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.29; H, 7.80; N, 11.74.

(+)- and (−)-*trans*-4-(Acetylamino)-1,3,4,5-tetrahydro-1-(*p*-tolylsulfonyl)benz[*cd*]indol-5-ol Mandelate (8 and 12). To a stirred suspension of **3** (11.4 g, 2.98 mmol), dicyclohexylcarbodiimide (7.2 g) and (−)-*O*-methylmandelic acid (6 g) in CH_2Cl_2 (400 mL) was added a catalytic amount of 4-(dimethylamino)-pyridine (500 mg) and stirring was continued for 1.5 h. The reaction mixture was filtered and then directly chromatographed (medium pressure) over silica gel (1.5 kg), using CH_2Cl_2–acetone (9:1) to elute. Evaporation afforded the pure isomers. The (+) isomer **8** (lower R_f) was obtained in 90% yield as a yellow foam which could not be crystallized: $[\alpha]_{Na}$ +58.8° (*c* 0.892, MeOH); NMR ($CDCl_3$) δ 1.83 (s, 3 H, $ArCH_3$), 2.36 (s, 3 H, $NCOCH_3$), 3.37 (s, 3 H, OCH_3), 4.56 (m, 1 H, H_4), 7.14 (t, 1 H, H_6).

Anal. Calcd for $C_{29}H_{28}N_2O_6S \cdot 1.25H_2O$: C, 62.75; H, 5.54; N, 5.05. Found: C, 62.64; H, 5.41; N, 5.10.

The (−) isomer **12** was obtained in 90% yield as a white solid which crystallized from CCl_4: mp 100–102 °C; $[\alpha]_{Na}$ −91.0° (*c* 1.0, MeOH); NMR ($CDCl_3$) δ 1.62 (s, 3 H, $ArCH_3$), 2.37 (s, 3 H, $NCOCH_3$), 3.38 (s, 3 H, OCH_3), 4.42 (m, 1 H, H_4), 7.22 (t, 1 H, H_6).

Anal. Calcd for $C_{29}H_{28}N_2O_6S \cdot 1.25H_2O$: C, 62.75; H, 5.54; N, 5.05. Found: C, 62.46; H, 5.62; N, 5.30.

(−)-*trans*-4-(Acetylamino)-1,3,4,5-tetrahydro-1-(*p*-tolylsulfonyl)benz[*cd*]indol-5-ol (13). To a stirred solution of KOH (1.3 g) in EtOH (60 mL) maintained at 50–55 °C was added the solid (−) ester **12** (8 g, 1.5 mmol) in one portion. Stirring was continued for 10 min and then the reaction mixture was poured into H_2O (250 mL). The product separated and was recovered by filtration and dried. The yield of **13** was 5.8 g (100%), mp 148 °C. Analytical material was crystallized from ethyl acetate: mp 184–186 °C; $[\alpha]_{Na}$ −77.9° (*c* 0.646, MeOH); NMR (Me_2SO-d_6) δ 1.77 (s, 3 H, $ArCH_3$), 2.32 (s, 3 H, $NCOCH_3$), 3.35 (s, 3 H, OCH_3), 4.66 (t, 1 H), 7.23–7.85 (8 H, ArH).

Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29. Found: C, 62.14; H, 5.62; N, 7.36.

(+)-*trans*-4-(Acetylamino)-1,3,4,5-tetrahydro-1-(*p*-tolylsulfonyl)benz[*cd*]indol-5-ol (9). The hydrolysis of the (+) ester **8** was carried out by exactly the same procedure described above for the (−) ester **12**. The yield of alcohol **9** was quantitative and the melting point of the analytical alcohol was 190–192 °C: $[\alpha]_{Na}$ +81.3° (*c* 0.772, MeOH); NMR (Me_2SO-d_6) δ 2.31 (s, 3 H, $ArCH_3$), 3.35 (s, 3 H, $NCOCH_3$), 4.66 (t, 1 H), 7.24–7.85 (8 H, ArH).

Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29. Found: C, 62.85; H, 5.41; N, 7.17.

(−)-*trans*-4,6,6a,7,9,10a-Hexahydro-7-ethylindolo[3,4-*gh*][1,4]benzoxazin-8-one (14). **14** was prepared by exactly the same procedure described for the preparation of racemate **4**. The yield of **14** was 66% and the pure material had the following: mp 276–278 °C dec (EtOH); $[\alpha]_{Na}$ −171.8° (*c* 0.74, DMF); NMR (Me_2SO-d_6) δ 1.11 (t, 3 H, CH_2CH_3), 4.35 (d, 1 H, J = 17 Hz), 4.42 (d, 1 H, J = 17 Hz), 5.1 (d, 1 H, J = 9 Hz), 6.92–7.24 (4 H, ArH).

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.08; H, 6.53; N, 10.80.

(+)-*trans*-4,6,6a,7,9,10a-Hexahydro-7-ethylindolo[3,4-*gh*][1,4]benzoxazin-8-one (10). **10** was prepared by exactly the same procedure described for the preparation of racemate **4**. The yield of **10** was 65% and the pure material had the following: mp 275–278 °C dec (EtOH); $[\alpha]_{Na}$ +165.47° (*c* 0.42, DMF); NMR (Me_2SO-d_6) δ 1.12 (t, 3 H, CH_2CH_3), 4.36 (d, 1 H, J = 17 Hz), 4.42 (d, 1 H, J = 17 Hz), 5.1 (d, 1 H, J = 9 Hz), 6.92–7.25 (4 H, ArH).

Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 69.91; H, 6.28; N, 10.52.

(−)-*trans*-4,6,6a,8,9,10a-Hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine (15). **15** was prepared by exactly the same procedure described for the preparation of racemate **5**. The yield of **15** was 64% and a pure sample had the following: mp 252–254 °C (THF; tube put in at 240 °C); $[\alpha]_{Na}$ −70.18° (*c* 0.778, DMF); NMR (Me_2SO-d_6) δ 1.0 (t, 3 H, CH_2CH_3), 4.56 (d, 1 H, J = 9 Hz), 6.87–7.16 (4 H, ArH), 10.7 (s, 1 H, NH).

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.18; H, 7.75; N, 11.79.

(+)-*trans*-4,6,6a,8,9,10a-Hexahydro-7-ethyl-7*H*-indolo[3,4-*gh*][1,4]benzoxazine (11). **11** was prepared by exactly the same procedure described for the preparation of racemate **5**. The yield of **11** was 61% and the pure material had the following: mp 252–255 °C (THF; tube put in at 240 °C); $[\alpha]_{Na}$ +69.57° (*c* 0.644, DMF); NMR (Me_2SO-d_6) δ 1.0 (t, 3 H, CH_2CH_3), 4.57 (d, 1 H, J = 9 Hz), 6.89–7.16 (4 H, ArH), 10.7 (s, 1 H, NH).

Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.39; H, 7.69; N, 11.72.

Acknowledgment. We are indebted to Mr. J. P. Moreau for chemical analyses, Dr. D. W. Cochran and Ms. J. S. Murphy for spectral data, Dr. G. E. Martin for confirmation of dopamine agonist activity, and Ms. T. H. Brunner for manuscript preparation.

Registry No. (±)-**1**, 81206-38-4; **2**, 81206-39-5; (±)-**3**, 81218-97-5; (±)-**4**, 81206-40-8; (±)-**5**, 77291-64-6; (±)-**6**, 81206-41-9; (±)-**7**, 81274-84-2; (±)-**8**, 81206-42-0; (±)-**9**, 81244-88-4; (±)-**10**, 81274-85-3; (±)-**11**, 81274-86-4; (−)-**12**, 81244-89-5; (−)-**13**, 81244-90-8; (−)-**14**, 81274-87-5; (−)-**15**, 81244-91-9; (−)-*O*-methylmandelic acid, 3966-32-3.