analog **8**. A general procedure is described (see Experimental Section) which permits direct conversion of the *o*-hydroxyamides into the 2-carbomethoxy-2-carbomethoxymethyl-2,3-dihydro-4*H*-1,3-benzoxazin-4-ones.

Biological Activity.[12]—Compounds **4, 5, 6, 7, 8, 10,** and **13** were evaluated for neuropharmacological activity in a modified Irwin mouse profile.[13] Materials were administered ip in solution or suspension in H_2O–methyl cellulose to 4 mice. Benzoxazinones **4**, **6**, and **7** were inactive up to 1000 mg/kg. The methoxysalicylamide adduct (**2**, R = H; R′ = 5-OMe) and its corresponding cyclized product **8** displayed slight depression at 300 mg/kg with marked writhing of the test animals observed in **8**.

The most significant activity, however, was observed in the halogenated benzoxazinones. Although the parent triiodosalicylanilide was exceedingly toxic, estimated LD_{50} 75 mg/kg, it did exhibit significant depression and reduction of spontaneous motor activity at doses as low as 30 mg/kg. The corresponding triiodobenzoxazine **10**, was considerably less toxic, no deaths occured at 300 mg/kg, and at this concentration the compounds displayed depression of alertness, reactivity, spontaneous motor activity, and muscle tone. Similar effects were observable in **5** at 1000 mg/kg and in **13** at 300 mg/kg.

Experimental Section[14]

Salicylamides and Salicylanilides.—Except as reported below these compounds were either commercial chemicals or were prepared by standard procedures available in the literature. 3,4′,5-Tribromosalicylanilide was obtained as a manufacturer's sample from Sherwin-Williams Chemical Co., and 3,5-dibromo-3′-trifluoromethylsalicylanilide was similarly obtained from Pfister Chemical Co.

4′-Bromosalicylanilide was prepared by treating a solution of 0.05 mole of salicylic acid and 0.05 mole of *p*-bromoaniline in 113 ml of PhCl with 0.024 mole of PCl_3 followed by 0.002 mole of $AlCl_3$. The mixture was stirred at reflux for 6 hr until HCl evolution ceased, cooled to room temperature, treated cautiously with 50 ml of H_2O and Na_3PO_4 (hydrate) until a slightly alkaline pH was achieved. Exhaustive steam distillation left an involatile white solid which was filtered from the chilled aq medium and recrystd from MeOH to give 12.6 g (86%) of 4′-bromosalicylanilide, mp 176.5–178°. *Anal.* ($C_{13}H_{10}BrNO_2$) C, H, N.

5-Methoxysalicylamide was prepared in 92% yield by allowing 0.10 mole of methyl 5-methoxysalicylate to stand in 160 ml of NH_3-satd MeOH for 1 week in a refrigerator. Concentration *in vacuo* precipitated the amide which was purified by recrystallization from MeOH, mp 148–151°. *Anal.* ($C_8H_9NO_3$) C, H, N.

3,4′,5-Triiodosalicylanilide and 3,5-diiodosalicylanilide[15] were prepared by the ICl iodination of 0.05 mole of salicylanilide in 160 ml of HOAc. A solution of 0.16 mole of ICl in 45 ml of HOAc was added dropwise to the above solution over 40 min. The addition of 200 ml of cold H_2O precipitated a tan solid and this mixture was heated to 75–90° with stirring for 1 hr, cooled to room temperature and the ppt collected by filtration. Recrystallization from HOAc yielded 3,4′,5-triiodosalicylanilide (mp 225–228°) in 23% yield. *Anal.* ($C_{13}H_8I_3NO_2$) N.

Dilution of the mother liquor yielded 45% of 3,5-diiodosalicylanilide, mp 165–168°, lit mp 173°.[15]

Benzoxazinone Synthesis.—To a solution containing 30 mmoles of the appropriate *o*-hydroxyamide and 3 mmoles of NaOMe in 50 ml of anhyd MeOH was added 33 mmoles of dimethyl acetylenedicarboxylate. The addition was carried out dropwise over 0.5–1 hr and the mixture was then allowed to stir at ambient temperature for 24 hr. Concentration *in vacuo* precipitated the white crystalline products which were recrystd from MeOH to analytical purity. Yields and physical properties are reported in Table I.

(12) Testing was carried out by Dr. T. O. King, Bio/dynamics Inc., East Millstone, N. J., and by Dr. Richard J. Matthews, Pharmakon Laboratories, Scranton, Pa.

(13) S. Irwin in "Animal and Clinical Pharmacologic Techniques in Drug Evaluation," J. H. Nodine and P. E. Siegler, Ed., Year Book Medical Publishers, Inc., Chicago, Ill., 1964.

(14) Melting points were obtained in capillaries in a Mel-Temp apparatus and are reported uncorrected. Elemental analyses were obtained from Dr. George I. Robertson, Microanalytical Laboratory, Florham Park, N. J., and where reported by the symbols of the elements are within ±0.3% of calculated values.

(15) Although the synthesis of these materials has been claimed in a patent, U. S. Patent 2,906,711; *Chem. Abstr.*, **54**, 3873 (1960), the details are insufficient to permit duplication of the method and a melting point is reported for only the 3,5-triiodosalicylanilide.

Substituted Oxindoles. III. Synthesis and Pharmacology of Some Substituted Oxindoles[1a]

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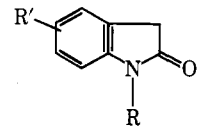
The compounds herein described were synthesized as part of a project complementary to an investigation of the alkaloids of various species of *Mitragyna*.[2] Certain investigators[3–6] have reported interesting pharmacological activity, whereas other workers[7,8] have found no significant activity among simple oxindole derivatives.



1, R = H (a) R′ = 4–OH; (b) R′ = 5–OH; (c) R′ = 6–OH; (d) R′ = 7–OH; (e) R′ = 4–MeO; (f) R′ = 5–MeO;
2, R = CH_3 (g) R′ = 6–MeO; (h) R′ = 7–MeO
8, (a) R = *n*-Pr; R′ = H; (b) R = *n*-Bu; R′ = H
10, R = Et; R′ = 5–OH
11a, R = Et; R′ = 6–OH; (b) R = *n*-Pr; R′ = 6–OH
12, R = Et; R′ = 5–MeO
13, R = Et; R′ = 6–MeO
19, R = H; (a) R′ = 4–EtO; (b) R′ = 4–*n*-PrO; (c) R = 4-*i*-PrO

Methods of preparation of compounds **1a–h** and **2a–h** have been described elsewhere.[2] The remaining compounds in this series were prepared by the routes shown in Schemes A and B. The appropriate substituted anilines **3a–c**, were acetylated and alkylated using NaH and the appropriate alkylating agent and deacetylated by refluxing with 50% H_2SO_4 to give the *N*-alkyl derivatives **5c–g** as oils. Reaction of these and the N-substituted anilines **6a,b** with $ClCH_2COCl$ and pyridine in

(1) (a) This work was carried out in part fulfilment of the requirements for the degree of Ph.D. of London University (R.W.D.); (b) Present address: School of Pharmacy, College of Technology, Brighton, Sussex, England.

(2) A. H. Beckett, R. W. Daisley, and J. Walker, *Tetrahedron*, **24**, 6093 (1968) and ref therein.

(3) M. Muller and R. S. Schmiedel, *Med. Exp.*, **11**, (3), 149 (1964).

(4) J. A. Orcutt, J. P. Prytherch, M. Konicov, and S. M. Michaelson, *Arch. Int. Pharmacodyn.*, **152**, 121 (1964).

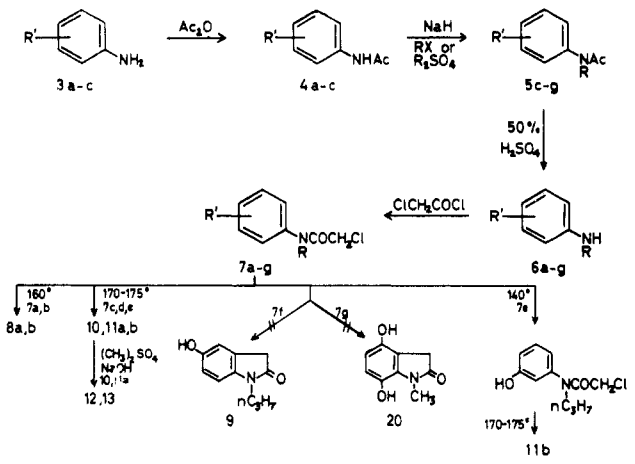
(5) M. E. Speeter, U. S. Patent 2,759,935 (1956). *Chem. Abstr.*, **51**, 2050c (1957).

(6) E. Merck A.-G. France M1657 (1963), *Chem. Abstr.*, **59**, 2777c (1963).

(7) F. Böhn, *Z. Physiol. Chem.*, **24**, 269 (1941).

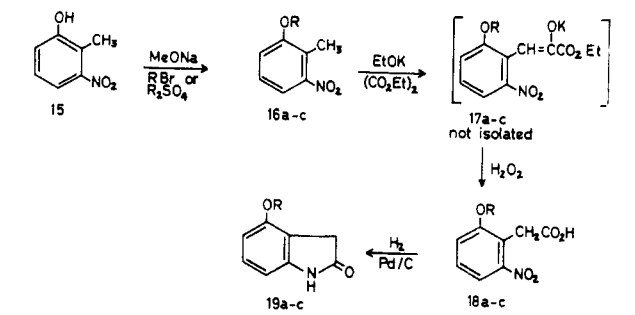
(8) G. N. Walker, R. T. Smith, and B. N. Weaver, *J. Med. Chem.*, **8**, 5, 626 (1965).

Scheme A



3 and 4, (a)R′ = *m*-CH_3O, (b)R′ = *p*-CH_3O, (c)R′ = 2,5-di-MeO
5–7, (a) R = *n*-Pr; R′ = H; (b) R = *n*-Bu; R′ = H; (c) R = Et; R′ = *m*-CH_3O; (d) R = Et; R′ = *p*-CH_3O; (e) R = *n*-Pr; R′ = *m*-CH_3O; (f) R = *n*-Pr; R′ = *p*-CH_3O; (g) R = Me; R′ = 2,5-di-MeO

Scheme B



16–19, R = (a) Et, (b) *n*-Pr, (c) *i*-Pr

C_6H_6 gave the chloroacetyl derivatives **7a–g** as viscous oils. Cyclization of these with anhyd $AlCl_3$ was as follows: **7a** and **7b** at a temperature of 160° gave *N*-*n*-propyl- and *N*-*n*-butyloxindole **8a** and **8b**, respectively, **8a** having been previously obtained from *N*-*n*-propyl-3,3-dibromooxindole with Zn and HCl.[9] At 170–175°, **7d** and **7c** furnished 5- and 6-hydroxy-*N*-ethyloxindoles (**10**, **11a**, subsequently methylated with Me_2SO_4 to give **12** and **13**). At the same temperature **7e** gave **11b**, whereas at 140°, it gave a Cl-containing compound soluble in NaOH and with ir absorption bands indicative of an OH group (3200 cm^{-1}) and a *meta* disubstituted benzene ring (797 and 708 cm^{-1}); this compound was assumed to be *N*-chloroacetyl-*N*-propyl-*m*-aminophenol (**14**) since on further heating with anhyd $AlCl_3$ to 170–175° it gave the oxindole **11b**. Attempts to cyclize **7f** and **7g** between 120 and 200° failed, probably due to the fact that the cyclization temperatures of the chloroacetyl compounds (or their demethylated homologs) were similar to the decomposition temperatures of the oxindoles.

Scheme B indicates the routes used for the synthesis of the 4-alkoxy-substituted oxindoles **19a–c**. 2-Hydroxy-6-nitrotoluene (**15**), prepared by an improved, previously described[2] method was alkylated with the appropriate alkyl halide or sulfate in the presence of MeONa to yield the ethers **16a–c**. Condensation of these with a twofold excess of diethyl oxalate and EtOK followed by treatment with alkaline H_2O_2 gave the phenylacetic acids **18a–c** in low yields. Pd-catalyzed reduction of these in the presence of AcOH or 5% NaOH gave the desired 4-substituted oxindoles **19a–c** in good yield.

Pharmacology.—None of the compounds showed any appreciable antiinflammatory or analgetic effects. Tetrabenazine antagonism was also absent. 4-Methoxyoxindole (**1e**) showed hypotonia and reduced motor activity, together with vasodilation, at 125 mg/kg in mice, the ED_{50} in the rotating rod test being 187 mg/kg. Following an oral dose of 300 mg/kg in mice, 5-methoxyoxindole (**1f**) produced ataxia with a slight to moderate decrease in smooth muscle action, the animals appearing normal after 2 hr. No tryptamine antagonism was found. 7-Methoxy-*N*-methyloxindole (**11h**) at an oral dosage of 100 mg/kg in mice produced decreased motor activity with low body posture, and at 300 mg/kg hypotonia and a loss of grasping reflex. At the latter dose level the onset of activity occurred within 15 min, reaching a peak at 2 hr and disappearing within 4 hr. 6-Methoxy-*N*-methyloxindole (**2g**) slightly augmented the pressor response to epirephrine, norepinephrine, and tyramine in the dog, but had no effect on resting blood pressure. 5-Hydroxy-*N*-methyloxindole (**2b**) likewise showed no significant cardiovascular effects in the dog.

Oxindole[3,4] and *N*-methyl- and *N*-ethyloxindole[4] have been reported as showing anticonvulsant and CNS depressant activity in mice and other animals, *N*-alkyl-3-phenyloxindoles as antispasmodics and analgetics,[5] while sedative and analgetic activity has been observed for some 5-alkoxy-oxindoles.[6] In view of these findings, the inactivity of the present series of compounds is disappointing, although other investigators have also found only slight activity among compounds of closely related types.[7,8]

Experimental Section

All spectra were recorded on a Perkin-Elmer Infracord 137 spectrophotometer. Microanalyses are by Dr. F. B. Strauss of Oxford, Dr. J. Baker, and Mr. R. Turner, School of Pharmacy, Brighton College of Technology. Melting points are corrected.

***N*-Alkylanisidines (6c–f).**—The appropriate acetylanisidine (**4a,b**, 33.0 g, 0.2 mole), prepared by standard methods was added slowly to refluxing Na-dried xylene (400 ml) containing NaH (10 g of 50% mineral oil dispersion). The thick white suspension was boiled under reflux (1 hr), stirring vigorously. Et_2SO_4 or 1-bromopropane (0.22 mole) was added dropwise to the boiling mixture. Boiling was continued for 1 hr (Et_2SO_4) or 24 hr (1-bromopropane), the product filtered, the xylene removed by reduced pressure distillation, and the residue hydrolyzed with boiling 50% w/v H_2SO_4 (250 ml, 6 hr). Neutralization of the product with 20% w/v NaOH gave the crude base which was Et_2O-extracted (3 × 100 ml). The Et_2O was dried ($MgSO_4$), filtered, and evaporated under reduced pressure and the residue vacuum distilled to yield **6c–f** as pale yellow oils.

***N*-Ethyl-*m*-anisidine (6c)** was obtained in 18.0 g (60%) yield: bp 95–96° (0.2 mm); lit.[10] bp 133–134° (12 mm). ***N*-Ethyl-*p*-anisidine (6d)** was obtained in 20.8 g (69%) yield: bp 86–88°

(9) A. Michaelis, *Ber.*, **30**, 2817 (1897).

(10) A. M. Hjort, E. J. deBeer, J. S. Buck, and W. S. Ide, *J. Pharmacol.*, **55**, 152 (1935).

(0.13 mm); lit.[11] bp 97° (0.3 mm). **N-Propyl-*m*-anisidine (6e)** was obtained in 25.2 g (76%) yield: bp 114–116° (0.13 mm); equiv wt 165.2. **N-Propyl-*p*-anisidine (6f)** was obtained in 18.5 g (56%) yield: bp 122–124° (0.1 mm); lit.[12] bp 65° (0.02 mm).

2,5-Dimethoxy-N-methylaniline (6g).—This was prepared as described above from 2,5-dimethoxy-*N*-acetylaniline (**4c**, 50 g, 0.26 mole); **6g** was obtained as a pale yellow oil: 30 g (71%); bp 120° (0.05 mm). The benzoyl derivative was obtained as white needles (EtOH–H_2O), mp 107–108°. *Anal.* ($C_{16}H_{17}NO_3$) C, H, N.

Chloroacetyl Derivatives 7a–g.—$ClCH_2COCl$ (8.5 ml, 0.11 mole) in dry C_6H_6 (40 ml) was added dropwise to a stirred, cooled solution of the *N*-alkylamine **6a–g** (0.1 mole) in dry C_6H_6 (100 ml) and anhydrous pyridine (8 ml). The mixture was stirred (2 hr), allowed to stand overnight at room temperature, and heated on a boiling water bath (0.5 hr). The cooled reaction mixture was treated with H_2O (80 ml) to dissolve precipitated salts, the C_6H_6 layer was separated and extracted with 2% w/v HCl (20 ml) followed by successive quantities (30 ml) of H_2O, until the aq layer was neutral. The C_6H_6 layer was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to yield the crude chloroacetyl derivatives **7a–g** as dark viscous oils which were used without further purification.

Cyclization of Chloroacetyl Derivatives 7a–g.—An intimate mixture of the chloroacetyl derivative with twice its weight of finely powdered anhyd $AlCl_3$ was heated for the time specified below, and the black solid or semisolid product when cold was decomposed with 2–3 times its weight of crushed ice. Weight of starting material, cyclization temperature, time, and work-up procedure after the addition of ice are as follows.

7a (21.1 g, 160°, 2 hr) was extracted with CH_2Cl_2 (3 × 50 ml) dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was distilled under high vacuum and the distillate recrystallized (petr ether 80–100°) to give ***N*-*n*-propyloxindole (8a)** as pale yellow prisms: 14.1 g (77%); bp 136° (0.05 mm); mp 68°; lit.[9] mp 68–69°.

The product (**7b**, 15.0 g, 160°, 2 hr) was worked up as for **7a** and distilled under high vacuum to give ***N*-*n*-butyloxindole (8b)** as a pale orange oil: 10.1 g (80%); bp 124–125° (1 mm). *Anal.* ($C_{12}H_{15}NO$) C, H, N.

After decomposition of **7d** (10, 50°, 10 min, 175°, 1 hr) with crushed ice the resulting solid was removed by filtration and after 3 recrystallizations (H_2O) gave **5-hydroxy-*N*-ethyloxindole (10)** as pale yellow needles: 4.5 g (58%); mp, 180–182°. *Anal.* ($C_{10}H_{11}NO_2$) C, H, N.

The crude (product of **7c** (10 g, 170°, 1 hr), recrystallized twice (H_2O), gave **6-hydroxy-*N*-ethyloxindole (11a)** as white needles: 3.7 g (48%); mp 174–175°. *Anal.* ($C_{16}H_{11}NO_2$) C, H, N.

The crude product of **7e** (5 g, 140°, 1 hr) removed by filtration and recrystallized twice (PhMe) gave slender white needles, 3.1 g, mp 160–161°, which were soluble in dil NaOH and gave a positive Cl test. The ir spectrum indicated the presence of OH (3200 cm^{-1}) and a *meta* disubstituted benzene ring (708, 797 cm^{-1}). It was formulated as ***N*-chloroacetyl-*N*-*n*-propyl-*m*-aminophenol (14)**, yield 64%. *Anal.* ($C_{14}H_{14}ClNO_2$) C, H, N.

The attempt to cyclize **7e** was repeated at 170° for 1 hr and the crude product was extracted with EtOH (50 ml), the resulting solution was filtered and treated twice with activated charcoal, refiltered, and evaporated to approximately 15 ml. Sandy prisms were deposited from this solution after several days at room temperature. These, when recrystallized (EtOH–H_2O) gave **6-hydroxy-*N*-propyloxindole (11b)** as long white needles: 1.6 g (13%); mp 169–171°. *Anal.* ($C_{11}H_{13}NO_2$) C, H, N. **11b** was also obtained by cyclization of **14** with anhydrous $AlCl_3$ at 170°.

All attempts to cyclize **7f** and **7g** with anhyd $AlCl_3$ at 120–200° were unsuccessful.

5-Methoxy-N-ethyloxindole (12).—Me_2SO_4 (2.2 g, 0.017 mole) was added dropwise to a cooled, stirred solution of 2.4 g (0.014 mole) of **10** in 7.5% w/v NaOH (9 ml). When the addition was complete the mixture was heated on a steam bath for 30 min, adding 7.5 w/v NaOH as necessary to maintain alkalinity. The product was cooled and extracted with Et_2O (3 × 20 ml), the Et_2O layer was dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue, recrystallized (petr ether 60–80°), gave pale yellow prisms: 2.0 g (78%); mp 75–76°. *Anal.* ($C_{11}H_{13}NO_2$) C, H, N.

6-Methoxy-N-ethyloxindole (13).—**11a** (3 g, 0.017 mole) was methylated as described in the previous experiment. Recrystallization (petr ether 80–100°) gave large slightly pink crystals: 2.2 g (68.0%); mp 65–66°. *Anal.* ($C_{11}H_{13}NO_2$) C, H, N.

2-Ethoxy-6-nitrotoluene (16a).—A solution of **15** (20 g, 0.13 mole) in MeOH (100 ml) was added to a solution prepared by dissolving Na (5.8 g, 0.25 g-atom) in MeOH (60 ml). Et_2SO_4 (34.2 g, 0.13 mole) was then added dropwise, stirring vigorously. When the addition was complete the mixture was boiled under reflux for 1 hr, most of the MeOH was removed by evaporation, the solution was diluted (H_2O, 100 ml) and extracted with Et_2O (3 × 50 ml). The Et_2O solution was washed successively with 5% w/v NaOH (50 ml) and H_2O (2 × 50 ml), dried ($MgSO_4$), filtered, and evaporated to dryness under reduced pressure. Vacuum distillation of the residue, followed by crystallization (MeOH–H_2O), gave pale yellow needles: 19.5 g (82%); bp 116° (2.2 mm); mp 48–49°. *Anal.* ($C_9H_{11}NO_3$) C, H, N.

2-*n*-Propoxy-6-nitrotoluene (16b).—This was prepared by a similar method to that described for **16a**, but using 1-bromopropane (32.9 g, 0.26 mole) as the alkylating agent with a reflux time of 4 hr. Vacuum distillation of the residue obtained from the Et_2O extract gave a product which when recrystallized (MeOH–H_2O) gave pale yellow plates: 12.3 g (48%); bp 180° (17 mm); mp 35–36°. *Anal.* ($C_{10}H_{13}NO_3$) C, H, N.

2-Isopropoxy-6-nitrotoluene (16c).—The method of preparation was similar to that used for **16b** using 2-bromopropane (32.9 g, 0.26 mole), and boiling under reflux for 12 hr. Vacuum distillation of the residue yielded a pale orange–yellow oil: 13.6 g (53%); bp 124° (2.2 mm). *Anal.* ($C_{10}H_{13}NO_3$) C, H, N.

2-Alkoxy-6-nitrophenylacetic Acids (18a–c).—To a suspension of EtOK prepared from K (7.8 g, 0.2 g-atom) and abs EtOH (25 ml) in dry Et_2O (160 ml) a solution of the appropriate alkoxynitrotoluene (**16a–c**) (0.1 mole) and diethyl oxalate (29.2 g, 0.2 mole) in dry xylene (50 ml) was added dropwise. The dark red–purple product was stirred for 4 hr and allowed to stand at room temperature for 3 days. The precipitated K salt (**17a–c**) was extracted with H_2O–ice (100 ml) and the resulting dark red aq layer extracted with Et_2O (3 × 50 ml), filtered, and the residual Et_2O removed by blowing air through the solution, which was then cooled in an ice bath and treated alternatively with 20% NaOH and 30% H_2O_2 (approx 16 ml of each) in small quantities until the dark red color was discharged. When subsequently filtered and acidified (concd HCl) the product was precipitated. **2-Ethoxy-6-nitrophenylacetic acid (18a)** was obtained as orange–brown needles (H_2O): 9.2 g (41%); mp 159°. *Anal.* ($C_{10}H_{11}NO_5$) C, H, N. **2-*n*-Propoxy-6-nitrophenylacetic acid (18b)** was obtained as pale yellow needles (H_2O): 6.9 g (32%); mp 133–134°. *Anal.* ($C_{11}H_{13}NO_5$) C, H, N. **2-Isopropoxy-6-nitrophenylacetic acid (18c)** was obtained as pale orange–yellow needles (H_2O): 2.6 g (11%); mp 157°. *Anal.* ($C_{11}H_{13}NO_5$) C, H, N.

4-Ethoxyoxindole (19a).—A solution of **18a** (2 g, 0.009 mole) in AcOH (40 ml) was hydrogenated at room temperature and pressure in the presence of 10% Pd–C (0.1 g). The theoretical uptake of H_2 was achieved after 1 hr, the product was filtered, the filtrate was evaporated to dryness under reduced pressure, and the residue was recrystallized (PhMe), to yield slender white needles: 1.2 g (80%); mp 197–198°. *Anal.* ($C_{10}H_{11}NO_2$) C, H, N.

4-*n*-Propoxyoxindole (19b).—A solution of **18b** (1.3 g, 0.0054 mole) in 5% NaOH solution (20 ml) was hydrogenated as for **19a**, the theoretical uptake of H_2 being achieved after 30 min. After filtration the product was acidified with concd HCl and heated on a steam bath for 30 min. On cooling, crystals appeared which when collected and recrystallized (EtOH–H_2O) gave white needles: 0.86 g (83%); mp 145–146°. *Anal.* ($C_{11}H_{13}NO_2$) C, H, N.

4-Isopropoxyoxindole (19c).—A solution of **18c** (2.4 g, 0.01 mole) in NaOH solution (30 ml) was hydrogenated as described above. Recrystallization of the product (EtOH–H_2O), gave fine white needles: 1.41 g (74%); mp 123–124°. *Anal.* ($C_{11}H_{13}NO_2$) C, H, N.

Acknowledgments.—We thank Smith, Kline and French Laboratories, Philadelphia, Pa., for pharmacological screening of the compounds. One of us, (R. W. D.) thanks the Pharmaceutical Society of Great Britain for a grant.

(11) Y. Nomura, *J. Chem. Soc. Jap. Pure Chem. Sect.*, **74**, 731 (1953).
(12) H. J. Barber and W. R. Wragg, *J. Chem. Soc.*, 610 (1946).