19462-65-8; II, X = Br, n = 6, 19462-66-9; III, n = 5, 19462-67-0; 7,8′-pentamethylene-1,4-methano-1,2,3,4-tetrahydropyrazolo[1,2-a]pyridozin-6-one, 19462-68-1; III, n = 6, 19462-69-2; X, 19462-70-5; XIII, 19462-71-6.

Acknowledgment.—This work was generously supported by grants from the U. S. Army Research Office (Durham). We are also indebted to P. H. Terry, D. J. Voaden, and G. Soldati for preliminary studies on the synthesis of some of the intermediates.

The Lithium Aluminum Hydride Reduction Products from Heterocycles Containing an Isoindolone Nucleus

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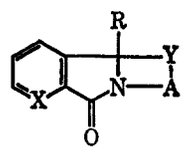
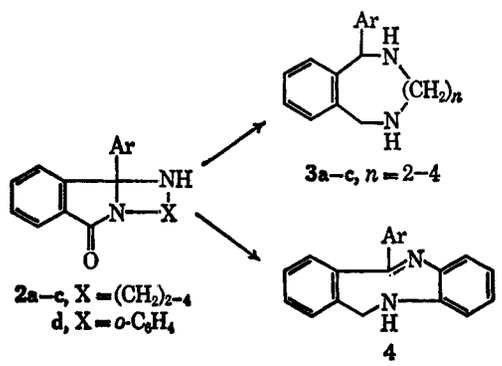
The lithium aluminum hydride reduction of a number of fused isoindolones (**1**) has been carried out in refluxing diethyl ether or tetrahydrofuran. Product composition was dependent on the type of heteroatom Y and the size of the fused ring A. All compounds where Y = O (**5a–c, 8, 11**) gave isoindolines as the major product while those with Y = NR (**13b** and **c, 26**) gave isoindoles. When Y = NH the products were either medium-sized heterocycles (**14** and **23**) or isoindoles (**15c** and **d, 19, 22a–c**). A mechanism is proposed to account for the variation in product composition.

Recent studies have demonstrated that the reaction of 2-alkanoyl or 2-aroylbenzoic acids with amino alcohols,[1a,b] diamines,[1b–g] mercaptoamines,[1b,h] anthranilic acid,[1i] anthranilamides,[1i] and salicylamides[1i] is a convenient method for preparing heterocycles containing an isoindolone nucleus. The types of ring systems that have been obtained by this procedure are exemplified by **1**.



1, A = $(CH_2)_{2-4}$, o-C_6H_4, o-COC_6H_4; R = alkyl, aryl; X = CH or N; Y = NH, NR, O, S

The lithium aluminum hydride ($LiAlH_4$) reduction of some ring systems of type **1** has recently been reported. Compounds **2a–c** are reported[1c,e,f,2] to give the medium-sized heterocycles **3a–c** while **2d**[3] is reported to give dibenzo[b,f][1,4]diazocines[1c] **4**.



(1) (a) T. S. Sulkowski, U. S. Patent 3,336,306 (Aug 15, 1967); (b) P. Aeberli and W. J. Houlihan, *J. Org. Chem.*, **34**, 165 (1969); (c) American Home Products Corp., Netherlands Patent Appl. 6,403,794 (1964); *Chem. Abstr.*, **63**, 9972 (1965); (d) J. R. Geigy, A.-G., Belgian Patent 659,530 (Aug 10, 1965); *Chem. Abstr.*, **64**, 664 (1966); (e) T. S. Sulkowski, M. A. Wille, A. Mascitti, and J. L. Diebolt, *J. Org. Chem.*, **32**, 2180 (1967); (f) W. Metlesics, T. Anton, and L. H. Sternbach, *ibid.*, **32**, 2185 (1967); (g) W. J. Houlihan, U. S. Patents 3,329,684 (July 4, 1967) and 3,334,113 (Aug 1, 1967); (h) J. R. Geigy, A.-G. Belgian Patent 659,528 (Aug 10, 1965); *Chem. Abstr.*, **64**, 3545 (1966); (i) P. Aeberli and W. J. Houlihan, *J. Org. Chem.*, **33**, 2402 (1968).

(2) Sandoz, Ltd., Netherlands Patent Appl. 6,614,399 (April 19, 1967); *Chem. Abstr.*, **68**, 3861 (1968).

(3) These compounds are incorrectly reported as 11-aryldibenzo[b,f][1,4]-diazocin-6(5H)-ones in ref 1c. Evidence for structure **2d** is given in ref 1b.

In this work we present our findings on the products obtained when various **1** are treated with excess lithium aluminum hydride in refluxing diethyl ether or tetrahydrofuran.

Reduction of oxazolo[2,3-a]isoindol-5(9bH)-one **5a** with excess $LiAlH_4$ in refluxing diethyl ether gave the known[3] **6a**. Treatment of oxazino[2,3-a]isoindol-6-one **5b** and oxazepino[2,3-a]isoindol-6-one **5c** in a similar manner gave hydroxyalkyl isoindolines **6b** and **6c**. In addition phthalimidine **7** was isolated from the reduction of **5c**. As with **6a** the three benzylic protons in **6b** and **6c** produced an $H_AH_BCNCH_C$ nmr pattern that exhibited long-range spin–spin interactions[4] between H_C and H_AH_B.

Reduction of isoindolo[1,2-b][1,3]benzoxazine-10,12-dione **8a** in refluxing tetrahydrofuran gave, after chromatography on silica gel, two products. The minor product was the known 3-methylphthalimidine **9a** and the major product has been assigned structure **10** based on nmr data. Reduction of the 9a-phenyl analog (**8b**) of **8a** gave as the only isolable product the known 3-phenylphthalimidine **9b**.

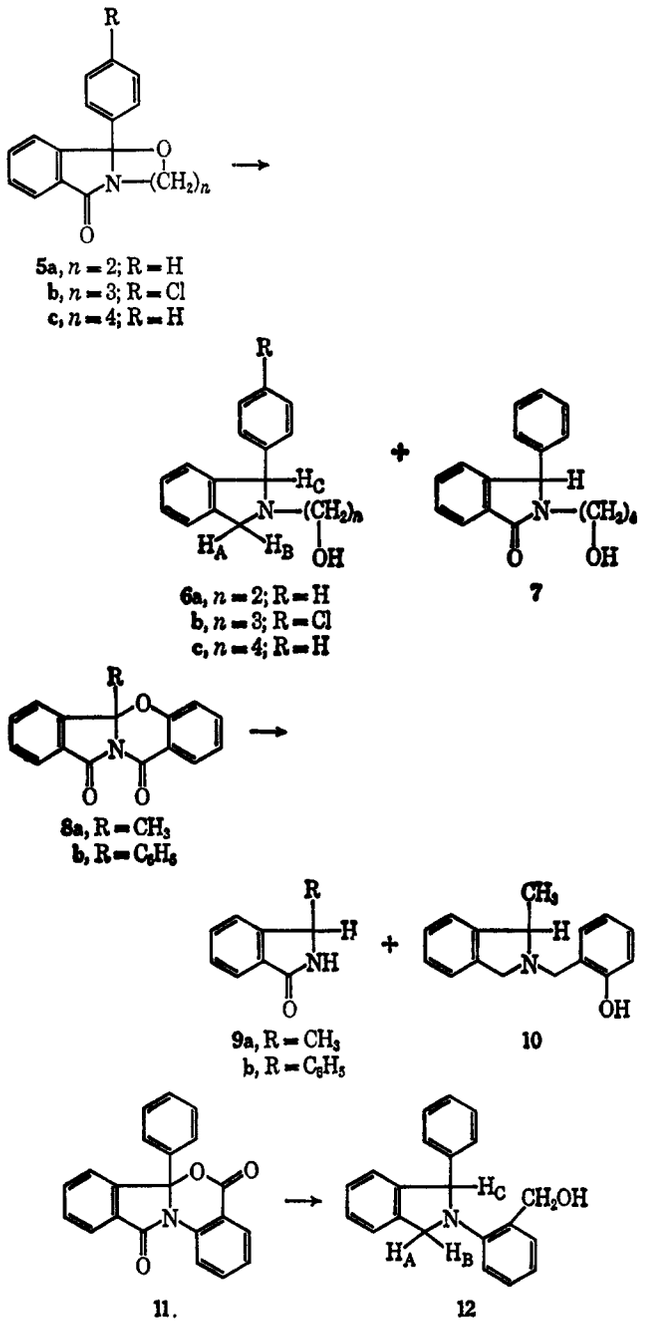
When **11** was reduced with LAH in refluxing tetrahydrofuran there were obtained after chromatography on silica gel two novel compounds in approximately equal quantities. The more polar substance was a blue oil that decomposed before identification could be completed. The nmr spectrum of the less polar compound gave the long-range coupled $CH_CNCH_AH_B$ system and other nmr data in agreement with isoindoline structure **12** (Chart I).

Treatment of imidazo[2,1-a]isoindol-5-one **13a** with $LiAlH_4$ in diethyl ether gave the previously reported[1e,2,5] 2,5-benzodiazocine **14a**. When the 1-methyl-9b-phenyl and 1-ethyl-9b-phenyl analogs (**13b–c**) of **13a** were reduced under similar conditions none of the eight-membered analogs of **14a** were obtained. Instead, the unstable 1-phenyl-2-N-alkylaminoethylisoindoles **15a**

(4) Long-range proton spin–spin interactions in the isoindoline system have been reported.[1b,e,f] A recent communication indicates the J values for this type of interaction is influenced by the group attached to the isoindoline nitrogen atom; J. T. Gerig, *Tetrahedron Lett.*, 4625 (1967).

(5) An independent synthesis of this compound has been given by D. H. Kim, A. A. Santilli, T. S. Sulkowski, and S. J. Childress, *J. Org. Chem.*, **32**, 3720 (1967).

CHART I

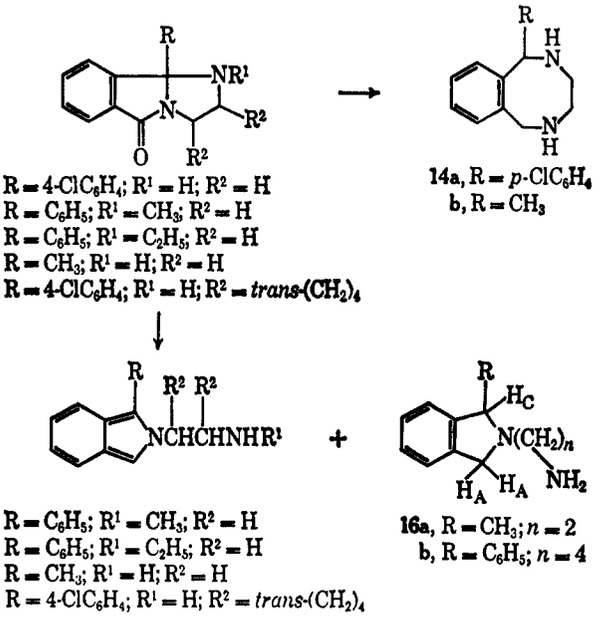


and **15b** were formed. Both of the compounds gave ultraviolet[6] and nmr data in agreement with an isoindole system.

Reduction of 9b-methyl analog **13d** gave an oil that afforded two products after distillation. The high-boiling component was identified as isoindole **15c.** The empirical formula of the low-boiling compound, $C_{11}H_{16}N_2$, agrees with either the eight-membered ring **14b** or isoindoline **16a.** The nmr showed a CH_3 doublet, a long-range coupled isoindoline $CH_AH_BNH_C$ system with further splitting of the H_C component by the methyl group, and other signals in agreement with the isoindoline structure **16a.** Further evidence for the isoindoline structure was obtained when **16a** gave a monoacetyl derivative on treatment with acetic anhydride in pyridine. *trans*-2,3-Tetramethylene analog **13e** gave isoindole **15d** when reduced with $LiAlH_4$ in diethyl ether (Scheme I).

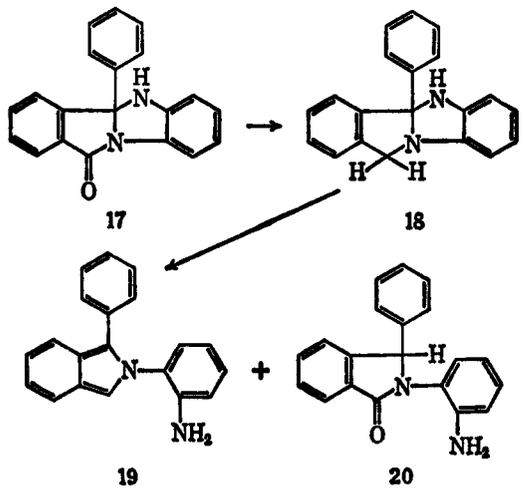
(6) D. F. Verber and W. Lwowski, *J. Amer. Chem. Soc.*, **86**, 4152 (1964); R. I. Fryer, J. V. Early, and L. H. Sternbach, *ibid.*, **88**, 3173 (1966).

SCHEME I



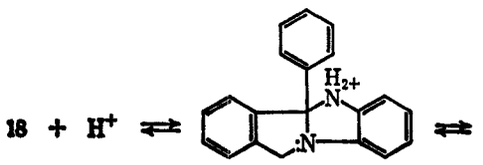
Reduction of isoindolo[2,1-*a*]benzimidazol-11-one **17** furnished an oil that gave an nmr spectrum with a 2 H AB system (J = 16 cps), one D_2O exchangeable H, and 13 aromatic protons. When the oil was dissolved in ethanol or $CHCl_3$ there was obtained a crystalline material. The nmr spectrum of this compound did not contain the AB system originally found in the oil but instead gave an nmr and uv spectrum in agreement with 1-phenyl-2-(*o*-aminophenyl)isoindole (**19**) (Scheme II).

SCHEME II

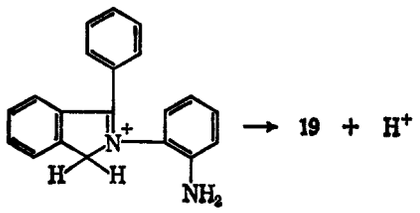


Apparently the oil, which we consider to be **18,** underwent a facile acid-catalyzed isomerization to the more stable isoindole system possibly *via* intermediates **18a** and **18b.** In a separate experiment where the crude oil was chromatographed on silica gel there was obtained **19** and 6% phthalimidine **20.** Our findings in the

reduction of **17** are inconsistent with those reported[1c] earlier since we did not obtain any compound corresponding to structure **4**.

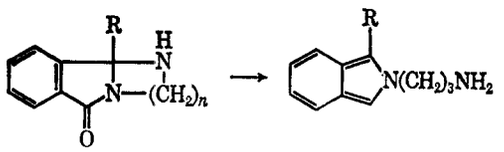


18a



18b

When pyrimido[2,1-*a*]isoindol-6(2H)-one **21a** was reduced with $LiAlH_4$ in diethyl ether there was obtained a compound that gave nmr and uv data in agreement with isoindole structure **22a**. This finding is also in disagreement with the report[1c] that compounds of **2b** are reduced to the nine-membered derivatives **3b**.

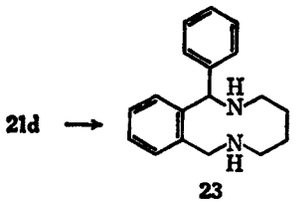


21a, R = 4-ClC_6H_4; $n = 3$
b, R = CH_3; $n = 3$
c, R = H; $n = 3$
d, R = C_6H_5; $n = 4$

22a, R = 4-ClC_6H_4
b, R = CH_3
c, R = H

Reduction of the 10b-methyl and 10b-hydrogen analogs **21b** and **c** also gave isoindole systems **22b** and **22c**, respectively.

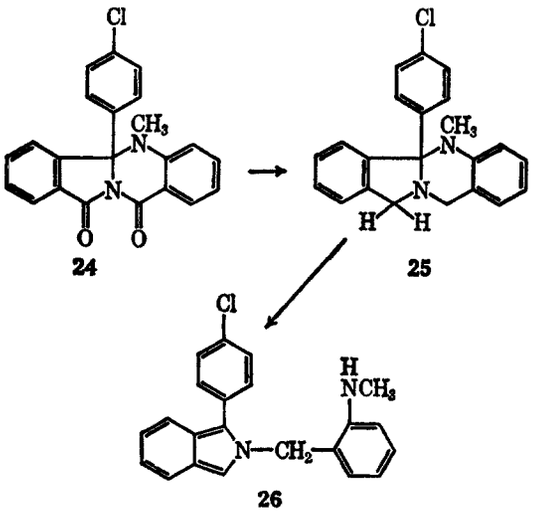
From the reduction of [1,3]diazepino[2,1-*a*]isoindol-7-one **21d** in diethyl ether there was obtained a compound that analyzed as **23** or **16b**. The nmr of this compound gave a 2 H AB system, a 1 H singlet, eight methylene, eight aromatic, and two D_2O exchangeable protons. The singlet AB arrangement[7] of the three benzylic protons is in agreement with structure **23** rather than **16b**[8] where the long-range coupled CH_AH_B-NCH_C would be expected. Additional evidence for the ten-membered ring structure was obtained when a diacetyl derivative was obtained from **23** and acetic anhydride.



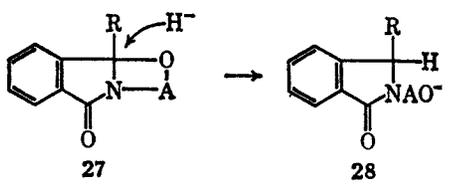
23

The reduction of isoindole[1,2-*b*]quinazoline-10,12-dione **24** in refluxing tetrahydrofuran afforded an oil that gave an nmr spectrum in agreement with structure **25**. When **25** was dissolved in methylene chloride–methanol or chromatographed on silica gel it formed an isomeric solid that gave an nmr and uv spectrum indicating isoindole structure **26**. The transformation **25** → **26** is similar to that of **18** → **19** and most likely proceeds by the same pathway (Scheme III).

SCHEME III



From the findings given above the reduction of fused isoindole **1** with excess $LiAlH_4$ in refluxing ether or tetrahydrofuran can give either an isoindoline, isoindole, or medium-sized ring. The reduction product depends on the heteroatom Y and for derivatives of **1** where Y is a NH or NR group the size and presence of substituents on the fused ring and the type of R group present on the bridgehead carbon will determine product composition. In all cases where Y is O (**5a–c**, **8a**, and **11**) the major reduction product is an isoindoline (**6a–c**, **10**, and **12**). The reduction pathway probably proceeds by a hydride attack on the C–O bond of **27** to form phthalimidine **28** which then undergoes amide carbonyl reduction to form



27 **28**

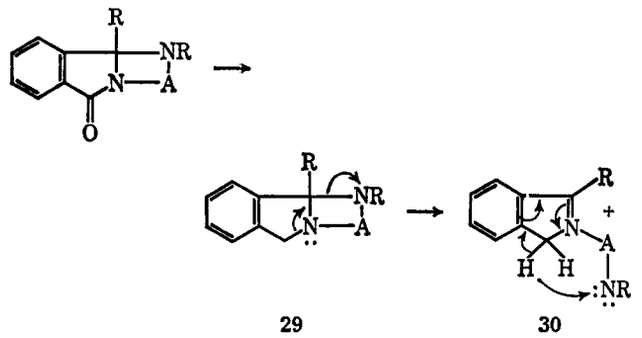
an isoindoline. Evidence for this pathway is supported by the isolation of the phthalimidine products **7** and **9a** and **b** from the reduction of **5c** and **8a** and **b** and the literature reports[1b,f,9] that $LiAlH_4$ reduction of 2-substituted phthalimidines gives isoindolines and not isoindoles. For the fused isoindolones where Y is NH or NR the reduction pathway is more complex. The compounds that form isoindoles (**13a–e**, **17**, **21a–d**, **24**)

(7) A similar pattern is found in the eight-membered compound **17a**; *cf.* ref 1e.

(8) This compound was incorrectly reported by W. J. H. to give **16b**; Sandoz S. A., French Patent 1,513,593 (Feb 2, 1968).

(9) (a) C. F. Huebner, U. S. Patent 3,031,458 (1962); *Chem. Abstr.*, **59**, 9989 (1963); (b) A. Pernot and A. Willemart, *Bull. Soc. Chim. Fr.*, 324 (1953).

are probably first reduced[10] at the amide carbonyl[11] to form fused isoindolines **29.** These compounds isomerize, possibly *via* intermediate **30,** in the reducing media or more likely during work-up to give the isoindoles. Support for this pathway is found in the reduction of **17** and **24** to **18** and **25** (analogs of **29**) and isomerization of these to **19** and **26.**

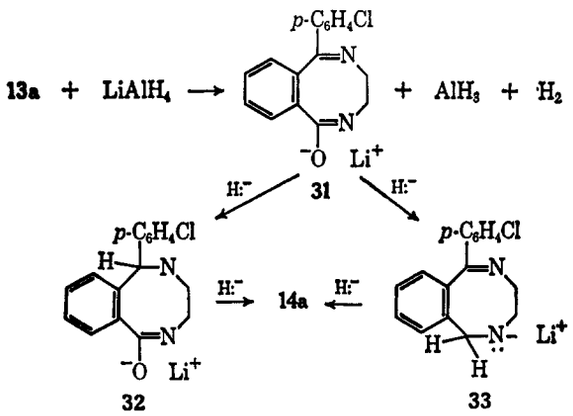


29 30

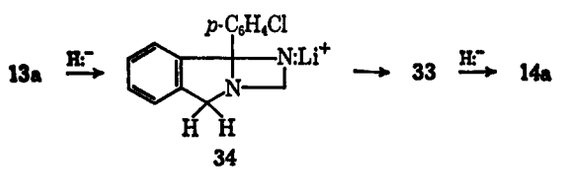
The formation of eight- and ten-membered ring compounds **14a** and **23** from **13a** and **21d** can be formulated in several ways. One mechanism[12] (Scheme IV) involves reaction of **13a** with $LiAlH_4$ to the isomerized[13] eight-membered ring anion **31.** Reduction of C=N or C=O to **32** or **33** followed by reduction of the remaining group leads to **14a.** A second pathway (Scheme V) requires reduction of the C=O group to the fused isoindoline anion **34** which undergoes isomerization to the eight-membered anion **33** and then reduction to **14a.** The third possibility (Scheme VI) involves the formation of the AlH_3 complex **35.** Hydride transfer to the bridgehead carbon atom accompanied by C–NCO bond cleavage leads to the eight-membered amide anion **33.** This anion can then be reduced at the amide carbonyl to form **14a.**

The three pathways given in Scheme IV–VI require that an NH group must be present for isomerization to occur and therefore agree with the observation that NCH_3 and NC_2H_5 analogs (**13b** and **c**) of **13a** do not give eight-membered ring compounds. That the isomerization is not dependent only on the presence of an NH group is clearly demonstrated by the reduction of **13d** and **e** to isoindoles **15c** and **d** rather than the eight-membered ring system. Schemes IV and V are very similar in that both require the reduction of a C=N bond (**31** or **33**) and C=O bond to form **14a** while Scheme VI requires the reduction of an iminal bond (**35**) and a C=O bond (**32**). Recent findings[14] in our laboratories have shown that the C=N bond in 1-(*p*-chlorophenyl)-6-methyl-4,5,6,7-tetrahydro-3H-2,6-benzodiazonine (**36**) is not reduced by $LiAlH_4$ under conditions that resulted in the formation of **14a** from **13a.** This result suggests that Schemes IV or V are not operative in forming **14a.** The formation[12] of **14a** probably occurs by the pathway given in Scheme VI.

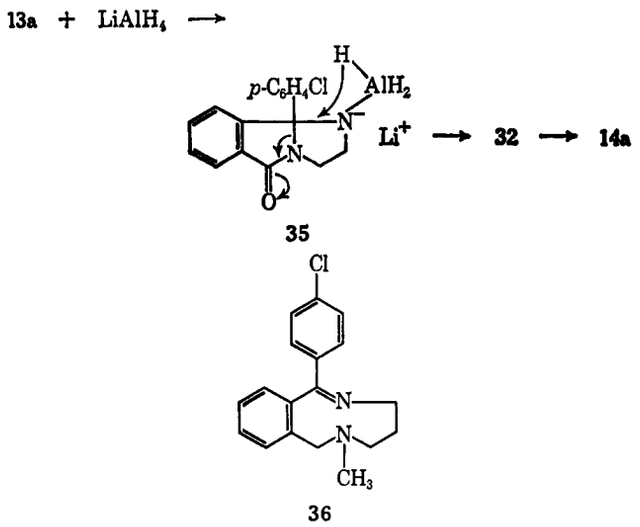
SCHEME IV



SCHEME V



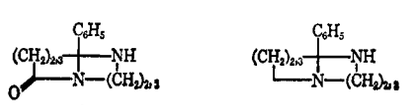
SCHEME VI



Experimental Section[15]

Synthesis of Fused Isoindolones.—Compounds **5a–c, 8a, b, 11, 13a, 17,** and **21b–d** have been reported in earlier literature.[1b,e,i]

(10) It is reported in ref 1b that the closely related fused lactams i are reduced by $LiAlH_4$ at the amide carbonyl to give the stable fused aminals ii.



i ii

(11) For a discussion on the mechanism of amide carbonyl reduction, see N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, New York, N. Y., 1956, p 546.

(12) For simplicity in formulation all mechanisms in Schemes IV–VI are given with **13a.** The same pathways are postulated for **21d.**

(13) A similar isomerization has been suggested by Sulkowski, *et al.*, in ref 1e to explain the formation of **14e.**

(14) W. J. Houlihan and R. E. Manning, First International Congress of Heterocyclic Chemistry, The University of New Mexico, Alburquerque, N. M., June 1967, Paper No. 37; *J. Org. Chem.*, in press.

(15) Melting points were determined on a Thomas–Hoover capillary melting apparatus and have not been corrected. Proton nmr spectra were obtained on a Varian Associates Model A-60 spectrometer and are expressed either in cycles per second (cps) or δ values (ppm) relative to a Me_4Si internal standard. Infrared spectra were determined in an appropriate solvent or as potassium bromide pellets using a Perkin-Elmer Infracord spectrophotometer. Ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, Model 15. Thin layer chromatography (tlc) was carried out on glass plates coated with silica gel HF-254, E. Merck AG.

TABLE I

PHYSICAL DATA FOR FUSED ISOINDOLONES

No.	Yield, %	Mp, °C	C=O, μ	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % N	Calcd, % O	Found, % C	Found, % H	Found, % N	Found, % O
5b[a]	82	140–142[b]	5.85	$C_{17}H_{14}ClNO_2$	68.1	4.7	4.7	10.7	68.1	4.9	4.6	10.6
13b	67	120–120[b]	5.90	$C_{17}H_{16}N_2O$	77.3	6.1	10.5	6.1	77.1	6.0	10.7	6.2
13c[c]	58	113–115[d]	5.89	$C_{18}H_{18}N_2O$	77.7	6.5	10.1	5.8	78.0	6.8	10.1	5.8
13d[e]	65	108–110[f]	5.84	$C_{11}H_{12}N_2O$	70.2	6.4	14.9		70.2	6.7	14.6	
13e	55	212–213[d]	5.86	$C_{20}H_{19}ClN_2O$	70.8	5.6	8.2	4.7	70.6	5.5	8.1	4.7
21a[j]	81	160–162	5.85	$C_{17}H_{15}ClN_2O$	68.3	5.1	9.4	5.4	68.7	5.5	9.3	5.5
24	51	209–210	5.68 5.97	$C_{22}H_{15}ClN_2O_2$	70.5	4.0	7.5	8.5	70.8	4.3	7.4	8.8

[a] Nmr ($CDCl_3$) δ 1.58 (2 H, m, $-CCH_2C-$), 3.08 (1 H, d-m, J = 13 cps, CH_ANCO), 3.92 (2 H, *m*, CH_2O), 4.50 (1 H, d-m, J = 13 cps, CH_BNCO), 7.43–786 (8 H, m, C_6H_4Cl and C_6H_4). [b] From CH_3OH–H_2O. [c] Nmr ($CDCl_3$) δ 0.99 (3 H, t, J = 7.0 cps, CH_3), 2.08 (2 H, m, CH_2NEt), 3.15 (3 H, m, $MeCH_2N$ and CH_ANCO), 3.85 (1 H, d-m, J = 13 cps, CH_BNCO), 7.08–792 (9 H), m, C_6H_5 and C_6H_4). [d] From ethanol–water. [e] Nmr ($CDCl_3$) δ 1.61 (3 H, s, CH_3), 2.00 (1 H, D_2O exchangeable, NH), 3.57 (4 H, m, NCH_2CH_2N), 7.32–7.61 (4 H, m, C_6H_4). [f] From diethyl ether. [g] Nmr ($CDCl_3$) δ 1.52 (2 H, m, $-CCH_2C-$), 1.92 (1 H, D_2O exchangeable, NH), 2.98.

Novel compounds have been prepared by published[1b,i] procedure and are listed in Table I.

General Procedure for Lithium Aluminum Hydride Reductions.—To a flask equipped with a Soxhlet extraction apparatus and maintained under a nitrogen blanket there was added anhydrous diethyl ether or tetrahydrofuran and lithium aluminum hydride and to the Soxhlet thimble there was added the isoindolone to be reduced. The mixture was stirred and refluxed and then cooled in an ice bath and treated with 2 *N* sodium hydroxide (2 ml/g of $LiAlH_4$), water (3 ml/g of $LiAlH_4$), and anhydrous sodium sulfate. The salts were filtered off and washed with diethyl ether or tetrahydrofuran. The filtrate was concentrated *in vacuo* and the resultant residue treated as indicated under the examples given below.

Reduction of 9b-Phenyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5-(9bH)-one (5a).—From 5.0 g (0.02 mol) of **5a**, 1.9 g (0.05 mol) of lithium aluminum hydride, and 100 ml of anhydrous diethyl ether (26 hr reflux) there was obtained 4.2 g of an oil. Distillation of this in a kugelrohr (180°, 0.5 mm) gave 3.9 g (81%) of 1-phenyl-2-(2-hydroxethyl)isoindoline[1b] (**6a**) as a viscous oil: ir ($CHCl_3$) 2.92 μ (OH); nmr ($CDCl_3$) δ 2.85 (2 H, m, CH_2N), 3.12 (1 H, D_2O exchangeable, OH), 3.58 (2 H, m, CH_2O), 3.78 (H_A), 4.52 (H_B), 4.79 (H_C, J_{AB} = 12 cps, J_{AC} = 3 cps, J_{BC} = 2 cps, $ArCH_AH_BNCH_CAr$).

Comparison of the infrared and nmr spectrum of **6a** prepared by $LiAlH_4$ reduction of 2-(2-hydroxyethyl)-3-phenylphthalimidine[1b] showed them to be identical.

Reduction of 10b-*p*-Chlorophenyl-3,4,6,10b-tetrahydro-2H-[1,3]oxazino[2,3-*a*]isoindol-6-one (5b).—From 25.0 g (0.083 mol) of **5b**, 7.9 g (0.20 mol) of lithium aluminum hydride, and 1000 ml of anhydrous diethyl ether (48 hr reflux) there was obtained 23.5 g of a semisolid substance that crystallized from methylene chloride–pentane (1:3) to give 22.2 g (91%) of 1-*p*-chlorophenyl-2-(3-hydroxypropyl)isoindoline (**6b**): mp 95–97°; R_f 0.45 ($CHCl_3$–CH_3OH, 98:2); ir (KBr) 2.95 and 2.98 μ (OH); nmr ($CDCl_3$) δ 1.68 (2 H, m, $-CCH_2C$), 2.82 (2 H, m, NCH_2C), 3.60 (1 H, D_2O exchangeable, OH), 3.61 (2 H, m, CH_2O), 3.68 (H_A), 4.53 (H_B), 4.58 (H_C, J_{AB} = 12 cps, J_{AC} = 3 cps, J_{BC} = 2 cps, $ArCH_AH_BNCH_CAr'$), 6.22–7.23 (8 H, m, C_6H_4Cl and C_6H_4); nmr ($CDCl_3$–CF_3COOH) δ 1.78 (2 H, m, $-CCH_2C$) 2.92 (2 H, m, CH_2N), 3.63 (2 H, m, CH_2O), 3.88 (H_A), 4.64 (H_B), 4.91 (H_C, J_{AB} = 13 cps, J_{AC} = 2 cps, J_{BC} = 2 cps, $ArCH_AH_BNCH_CAr'$) 6.81–7.32 (8 H, m, C_6H_4Cl and C_6H_4).

Anal. Calcd for $C_{17}H_{18}ClNO$: C, 71.0; H, 6.3; Cl, 12.4; N, 4.9; O, 5.6. Found: C, 71.1; H, 6.5; Cl, 12.4; N, 5.0; O, 5.6.

A solution of 693 mg of **6b**, 2.7 ml of dry pyridine and 2.2 ml of acetic anhydride was refluxed for 3 hr and processed in the usual manner to give 500 mg of the acetate of **6b** as an oil: R_f 0.60 ($CHCl_3$–CH_3OH, 98:2); ir (CH_2Cl_2) 5.81 μ (C=O); nmr ($CDCl_3$) δ 1.90 (3 H, s, CH_3), 1.92 (2 H, m, CH_2), 2.68 (2 H, t, J = 6.0 cps, CH_2N), 4.05 (2 H, t, J = 6.0 cps, CH_2O), 3.73 (H_A), 4.47 (H_B), 4.75 (H_C, J_{AB} = 12 cps, J_{AC} = 2.0 cps, J_{BC} = 2.0 cps, $ArCH_BH_PNCH_CAr'$), and 6.80–7.40 (8 H, m, aromatic protons).

Anal. Calcd for $C_{19}H_{20}ClNO_2$: C, 69.1; H, 6.1; O, 9.8. Found: C, 69.3; H, 6.0; O, 9.7.

Reduction of 11b-Phenyl-2,3,4,5,7,11b-hexahydro[1,3]oxazepino[2,3-*a*]isoindol-7-one (5c).—From 6.9 g (0.025 mol) of **5c**, 2.4 g (0.063 mol) of lithium aluminum hydride, and 500 ml of anhydrous diethyl ether (72 hr reflux) there was obtained 6.5 g of an oil; tlc on silica gel ($CHCl_3$–CH_3OH 95:5) gave R_f 0.42 and 0.48. Chromatography on silica gel (60 g) gave fraction 1 [3.6 g, (eluent, C_6H_6–$CHCl_3$ 80:20), R_f 0.42] and fraction 2 [2.4 g (eluent, $CHCl_3$), R_f 0.48]. Crystallization of fraction 1 from isopropyl alcohol–water gave 1-phenyl-2-(4-hydroxybutyl)isoindoline (**6c**): mp 72–74°; ir (CH_2Cl_2) 2.78 and 3.15 μ (OH); nmr ($CDCl_3$) δ 1.58 (4 H, m, $-CCH_2CH_2C-$), 2.70 (2 H, m, NCH_2), 3.48 (2 H, t, J = 6.0 cps, CH_2O), 3.95 (1 H, OH), 3.72 (H_A), 4.49 (H_B), 4.73 (H_C, J_{AB} = 12 cps, J_{AC} = 2.0 cps, $ArCH_AH_BNCH_CAr'$), 6.82–7.52 (9 H, m, aromatic H).

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.9; H, 7.9; N, 5.2; O, 6.0. Found: C, 80.6; H, 8.1; N, 5.2; O, 5.9.

Fraction 2 was distilled in a kugelrohr (180°, 0.2 mm) to give 1.9 g of 2-(4-hydroxybutyl)-3-phenylphthalimidine (**7**): ir (CH_2Cl_2) 2.77 and 2.94 (OH), 5.91 μ (C=O); nmr ($CDCl_3$) δ 1.62 (4 H, m, $C-CH_2CH_2-C$), 2.98 (1 H, m), 3.68 (3 H, m), 3.73 (1 H, D_2O exchangeable, OH), 5.79 (1 H, s, CH), 7.28 (8 H, m, C_6H_3 and C_6H_5), 7.88 (1 H, m, =CHCO).

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.8; H, 6.8; N, 5.0. Found: C, 76.8; H, 7.1; N, 4.9.

Reduction of 5a-Methyl-11,12-dihydro-5aH-isoindolo[1,2-*b*]-[1,3]benzoxazine-10,12-dione (8a).—From 12.0 g (0.045 mol) of **8a**, 8.6 g (0.23 mol) of lithium aluminum hydride, and 500 ml of anhydrous tetrahydrofuran (18 hr reflux) there was obtained 12.8 g of an orange oil ($CHCl_3$–CH_3OH 98:2), R_f 0.25 and 0.80. Chromatography of a 6.0-g sample of the oil on a silica gel column ($CHCl_3$ eluent) gave fraction 1 (4.7 g, R_f 0.80), fraction 2 (1.2 g, R_f 0.25), and fraction 3 (0.2 g, R_f 0.90 and 0.3). Fraction 3 was not studied. Fraction 2 was crystallized from methylene chloride–diethyl ether–pentane to give 0.158 g of 3-methylphthalimidine (**9a**): mp 112–114° (lit.[16] mp 110–111°); nmr ($CDCl_3$) δ 1.52 (3 H, d, J = 6.5 cps, CH_3), 4.74 (1 H, q, J = 6.5 cps, CH), 8.60 (1 H, D_2O exchangeable CONH), and 7.27–8.00 (4 H, m C_6H_4). Fraction 1 was crystallized from methylene chloride–pentane to give 4.2 g of 1-methyl-2-(*o*-hydroxybenzyl)isoindoline (**10**): mp 105–108°; ir (KBr) 2.95 μ (OH); uv maxima 266 mμ (ϵ 2740) and 272 (3670); nmr ($CDCl_3$) δ 1.52 (3 H, d, J = 6.5 cps, CH_3), 3.63 (H_A), 4.41 (H_P, J = 12 cps, NCH_AH_BArOH), 3.98 (H_C), 4.18 (H_A), 4.32 (H_C, J_{AB} = 13 cps, J_{AC} = 1.5 cps, J_{C-CH_3} = 7 cps, $CH_CNCH_AH_B$), 6.68–7.36 (8 H, m, $C_6H_4C_6H_4$), 8.55 (1 H, D_2O exchangeable, OH).

Anal. Calcd for $C_{16}H_{17}NO$: C, 80.3; H, 7.1; N, 5.9; O, 6.7. Found: C, 80.5; H, 7.4; N, 5.9; O, 6.8.

Reduction of 5a-Phenyl-11,12-dihydro-5aH-isoindolo[1,2-*b*]-

(16) A. Rosenthal, R. F. Astbury, and A. Hubscher, *J. Org. Chem.*, **23**, 1037 (1958).

[1,3]benzoxazine-10,12-dione (8b).—From 3.0 g (0.0092 mol) of **8b**, 1.1 g (0.029 mol) of lithium aluminum hydride, and 250 ml of anhydrous tetrahydrofuran (24 hr reflux) there was obtained 2.7 g of a blue oil. Crystallization from ethanol gave 0.95 g of 3-phenylphthalimidine (**9b**): mp 225–227° (lit.[17] mp 220°); ir (KBr) 2.95 (NH), 5.91 μ (C=O); nmr (C_2D_6SO) δ 5.73 (1 H, s, ArCHAr'), 7.20–7.90 (9 H, m, C_6H_4 and C_6H_5), 9.05 (1 H, D_2O exchangeable, CONH).

Concentration of the filtrate from **9b** gave a blue oil that rapidly darkened to an intractable tar.

Reduction of 6a-Phenyl-6a,11-dihydro-5H-isoindolo[2,1-a]-[3,1]benzoxazine-5,11-dione (11).—From 13.0 g (0.04 mol) of **11**, 7.6 g (0.20 mol) of lithium aluminum hydride, and 750 ml of anhydrous tetrahydrofuran (56 hr reflux) there was obtained 12.2 g of a dark brown oil, R_f 0.20 and 0.40 ($CHCl_3$–CH_3OH 95:5). Chromatography on silica gel (240 g) gave fraction 1 [6.1 g (eluent C_6H_6–$CHCl_3$ 1:1), R_f 0.40], fraction 2 [0.8 g (eluent $CHCl_3$), R_f 0.40 and 0.20], and fraction 3 [6.0 g (eluent, $CHCl_3$–CH_3OH 98:2)].

Fraction 1 was crystallized from diethyl ether–pentane to give 1-phenyl-2-(*o*-hydroxymethylphenyl)isoindoline (**12**): mp 83–86°; ir (CH_2Cl_2) 2.78 and 2.93 μ (OH); uv maxima 258 mμ (ϵ 6690), 263 sh (6020), and 272 sh (4460); nmr ($CDCl_3$) δ 3.75 (1 H, D_2O exchangeable, OH), 4.33 (H_A) and 4.78 (H_B, J = 13.0 cps, CH_AH_BO), 4.38 (H_A), 4.95 (H_B), 5.89 (H_C, J_{AB} = 13.0 cps, J_{AC} = 1.5 cps; $ArCH_AH_BNCH_CAr'$), 6.83–7.45 (13 H, m, aromatic H).

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.7; H, 6.4; O, 5.3. Found: C, 83.4; H, 6.6; O, 5.6.

Fraction 2 was not studied. Fraction 3 could not be identified because it rapidly decomposed to a dark brown tar.

Reduction of 1-Methyl-9b-phenyl-1,2,3,9b-tetrahydro-5H-imidazo[2,1-a]isoindol-5-one (13b).—From 6.0 g (0.023 mol) of **13b**, 2.2 g (0.058 mol) of lithium aluminum hydride, and 500 ml of anhydrous diethyl ether (30 hr reflux) there was obtained 5.7 g of a pale yellow oil. Distillation in a kugelrohr (180°, 0.5 mm) gave 5.1 g (89%) of 1-phenyl-2-methylaminoethylisoindole (**15a**): $n^{20}D$ 1.6629; ir (CH_2Cl_2) 2.76 and 3.02 (NH_2), 6.25 and 7.50 μ; uv maxima 222 mμ (ϵ 30,000), 272 (5200), 283 (5200), 320 infl (5200) and 345 (7600); nmr ($CDCl_3$) δ 0.88 (1 H, D_2O exchangeable, NH), 2.17 (3 H, s, NCH_3), 2.74 (2 H, t, J = 6.0 cps, CH_2N), 4.24 (2 H, t, J = 6.0 cps, N^2CH_2), 7.15 (1 H, s, CCHN), and 6.91–7.65 (9 H, m, C_6H_5 and C_6H_4).

Anal. Calcd for $C_{17}H_{18}N_2$: C, 81.6; H, 7.3; N, 11.2. Found: C, 81.0; H, 7.5; N, 11.6.

Reduction of 1-Ethyl-9b-phenyl-1,2,3,9b-tetrahydro-5H-imidazo[2,1-a]isoindol-5-one (13c).—From 5.0 g (0.018 mol) of **13c**, 1.7 g (0.045 mol) of lithium aluminum hydride, and 500 ml of anhydrous diethyl ether (16 hr reflux) there was obtained 5.1 g of an oil, R_f 0.23 and trace at 0.56 ($CHCl_3$–CH_3OH 95:5). Distillation through a Vigreux column gave 3.6 g (75%) of 1-phenyl-2-(2-ethylaminoethyl)isoindole (**15b**): bp 185–190° (0.5 mm); $n^{20}D$ 1.6610; uv maxima 274 mμ (ϵ 5300), 285 (5000), 345 (8000); nmr (CCl_4) δ 0.91 (3 H, t, J = 7.0 cps, CH_3), 1.26 (1 H, D_2O exchangeable, NH), 2.40 (2 H, q, J = 7.0 cps, NCH_2Me), 2.75 (2 H, t, J = 6.0 cps, CH_2N), 4.16 (2 H, t, J = 6.0 cps, CH_2N=), 7.32 (1 H, s, C=CHN), 7.25 (9 H, m, C_6H_5 and C_6H_4).

Anal. Calcd for $C_{18}H_{20}N_2$: C, 81.8; H, 7.6; N, 10.6. Found: C, 81.6; H, 7.5; N, 10.7.

Reduction of 9b-Methyl-1,2,3,9b-tetrahydro-5H-imidazo[2,1-a]isoindol-5-one (13d).—From 8.0 g (0.046 mol) of **13d**, 4.3 g (0.116 mol) of lithium aluminum hydride and 500 ml of anhydrous diethyl ether (56 hr reflux) there was obtained 7.8 g of a liquid, R_f 0.26 and 0.55 ($CHCl_3$–CH_3OH 80:20). Distillation (nitrogen atmosphere) gave fraction 1 [3.8 g, bp 92° (0.50 mm), $n^{20}D$ 1.5572, R_f 0.26], fraction 2 [0.4 g, bp 92–123°, $n^{20}D$ 1.5813, R_f 0.26 and 0.55], and fraction 3 [3.5 g, bp 123° (0.50 mm), $n^{20}D$ 1.6257, R_f 0.55].

Fraction 1 was identified as 1-methyl-2-aminoethylisoindoline (**16a**): nmr ($CDCl_3$) δ 1.43 (3 H, d, J = 6.0, CH_3), 1.45 (2 H, D_2O exchangeable, NH_2), 2.82 (4 H, m, NCH_2CH_2N), 3.54 (H_A), 3.83 (H_B), 4.31 (H_C, J_{AB} = 13.0 cps, J_{AC} = 2.0 cps, J_{BC} = 2.0 cps, $ArCH_HH_PNCH_C$).

(17) G. Caronna and S. Palazzo, *Gazz. Chim. Ital.*, **83**, 308 (1953); *Chem. Abstr.*, **47**, 12294 (1953).

Anal. Calcd for $C_{11}H_{16}N_2$: C, 75.4; H, 8.6; N, 16.0. Found: C, 75.2; H, 8.4; N, 16.1.

Fraction 2 was not studied. Fraction 3 was identified as 1-methyl-2-aminoethylisoindole (**15c**): ir (CH_2Cl_2) 2.73 and 2.95 μ (NH_2); uv maxima 227 mμ (ϵ 22,500), 269 (2250), 280 (2010), 341 (2200), 404 (450), 428 (600), and 443 (750); nmr ($CDCl_3$) δ 1.23 (2 H, D_2O exchangeable, NH_2), 2.48 (3 H, s, CH_3), 2.96 (2 H, t, J = 6.0 cps, CH_2N, 4.07 (2 H, t, J = 6.0 cps, CH_2N), 6.97 (1 H, s, NCH=), 6.83 (2 H), and 7.44 (2 H, A_2B_2 multiplet, C_4H_4).

Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.8; H, 8.1. Found: C, 75.7; H, 8.1.

A solution of 0.90 g of **16a**, 1.0 ml of acetic anhydride, and 5 ml of pyridine was allowed to stir for 15 hr under a nitrogen atmosphere. The dark colored solution was concentrated *in vacuo*, dissolved in chloroform and washed with cold sodium bicarbonate solution. The solvent was removed *in vacuo* and the residue distilled in a kugelrohr (150°, 0.5 mm) to give 0.70 g of 1-methyl-2-(acetamidoethyl)isoindoline: nmr ($CDCl_3$) δ 1.41 (3 H, d, J = 6.0 cps, CH_3), 1.97 (3 H, s, CH_3CO), 2.40–4.00 (5 H, m, CH_2CH_2 and CH_AN), 3.58 (H_B), 4.28 (H_C, J_{AB} = 13.0 cps, J_{AC} = 2.0 cps, $ArCH_AH_BNCH_C$), 6.32 (1 H, D_2O exchangeable, NH), and 7.28 (4 H, m, C_6H_4).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 79.2; H, 8.6; O, 8.1. Found: C, 79.0; H, 8.4; O, 8.0.

Reduction of *trans*-4-*p*-Chlorophenyl-4a,5,6,7,8,9-hexahydroisoindolo[2,1-a]-11H-benzimidazol-11-one (13e).—From 8.5 g (0.025 mol) of **13e**, 1.9 g (0.05 mol) of lithium aluminum hydride and 200 ml of anhydrous diethyl ether (18 hr reflux) there was obtained 6.7 g of a blue oil that gave 2.9 g of 1-*p*-chlorophenyl-2-(*trans*-2-aminocyclohexyl)isoindole (**15d**): mp 119–120° (pentane–diethyl ether); ir (CH_2Cl_2) 2.73, 2.78, 2.96 (NH_2), 6.65, 7.42, 8.16, 9.10 μ; uv maxima 224 mμ (ϵ 40,850), 275 (4900), 286 (5034), 348 (12,465); nmr ($CDCl_3$) δ 0.92 (2 H, D_2O exchangeable, NH_2), 1.62 [8 H, m, $(CH_2)_4$], 3.04 (1 H, m, CHN), 3.88 (1 H, m, CHN^2), 6.91 (2 H, m, C_4HC_7H), 7.27 (1 H, s, =CHN), 7.42 (6 H, broad s, C_6H_4 and C_5HC_6H).

Anal. Calcd for $C_{20}H_{21}ClN_2$: C, 73.6; H, 6.5; Cl, 10.9; N, 8.6. Found: C, 74.0; H, 6.8; Cl, 10.8; N, 8.8.

Reduction of 4a-Phenyl-4a,5-dihydro-11H-isoindolo[2,1-a]-benzimidazol-11-one (17).—From 15.0 g (0.05 mol) of **17**, 4.8 g (0.13 mol) of lithium aluminum hydride, and 500 ml of anhydrous diethyl ether (18 hr reflux) there was obtained 14.5 g of 4a-phenyl-4a,5-dihydro-11H-isoindolo[2,1-a]benzimidazole (**18**) as a pale yellow oil: R_f 0.95 ($CHCl_3$–CH_3OH 98:2); nmr ($CDCl_3$) δ 4.30 (H_A) 4.61 (H_B, J = 16 cps, CH_AH_B), 4.35 (NHD_2O exchangeable), 6.50–7.70 (13 H, m, aromatic H). Chromatography of **18** (14.1 g) on silica gel (200 g) gave 13.4 g of solid A ($CHCl_3$ eluent; R_f 0.90, $CHCl_3$–CH_3OH 98:2) and 0.9 of solid B ($CHCl_3$–CH_3 98:2 eluent; R_f 0.05, $CHCl_3$–CH_3OH, 98:2). Recrystallization of A from methanol–methylene chloride gave 11.3 g of 1-phenyl-2-(*o*-aminophenyl)isoindole (**19**): mp 142–145°; ir (KBr) 2.88 and 2.96 (NH_2), 6.18 and 7.20 μ; uv maxima 215 mμ (ϵ 33,560), 284 (7350), 304 (7350), 320 infl (6445), and 350 (6445); nmr ($CDCl_3$) δ 3.42 (2 H, D_2O exchangeable, NH_2), 7.00 (1 H, s, C=CHN–) and 6.50–7.70 (13 H, m, aromatic H).

Anal. Calcd for $C_{20}H_{16}N_2$: C, 84.6; H, 5.6; N, 9.8. Found: C, 84.4; H, 5.9; N, 9.8.

The solid B was crystallized from methanol to give 0.6 g of 2-(*o*-aminophenyl)-3-phenylphthalinidine (**20**): mp 190–192°; ir (KBr) 2.92 and 2.98 (NH_2), 6.00 (C=O), 6.18 and 7.20 μ; nmr ($CDCl_3$) δ 3.88 (2 H, D_2O exchangeable, NH_2), 6.02 (1 H, s, CHN), 6.78 (4 H, q, NC_6H_4N), 7.07–7.59 (8 H, m, C_6H_5 and C_6H_4), 8.92 (1 H, m, HC=CCO).

Anal. Calcd for $C_{20}H_{16}N_2O$: C, 80.0; H, 5.3; O, 5.3. Found: C, 80.2; H, 5.1; O, 5.4.

Reduction of 10b-*p*-Chlorophenyl-1,3,4,10b-tetrahydropyrimido[2,1-a]isoindol-6(2H)-one (21a).—From 15.0 g (0.05 mol) of **21a**, 5.0 g (0.13 mol) of lithium aluminum hydride, and 500 ml of anhydrous diethyl ether (48 hr reflux) there was obtained 14.4 g (92%) of 1-*p*-chlorophenyl-3-aminopropylisoindole (**22a**) as a yellow oil: ir (CH_2Cl_2) 2.75 and 2.98 μ (NH_2); uv maxima 222 mμ (ϵ 29,910), 274 (3870), 280 (3870), and 349 (9150); nmr ($CDCl_3$) δ 1.02 (2 H, D_2O exchangeable, NH_2), 1.74 (2 H, m, CCH_2C), 2.46 (2 H, t, J = 7.0 cps, CH_2N–), 4.23 (2 H, t, NCH_2), 7.16 (1 H, s, =CHN), 7.39 and 7.51 (4 H, A_2B_2 pattern, HC=CHCH=CH). On exposure to air or light **27a** very rapidly darkened.

A solution of 7.2 g of **22a** in 250 ml of anhydrous diethyl ether was cooled in an ice bath and then treated with a stream of dry hydrogen chloride gas. The resultant solid was filtered off and recrystallized from 95% ethyl alcohol. There was obtained 4.4 of **22a**·HCl, mp 260–262°.

Anal. Calcd for $C_{17}H_{18}N_2Cl_2$: C, 63.6; H, 5.6; Cl, 22.1; N, 8.7. Found: C, 63.8; H, 5.8; Cl, 21.9; N, 8.9.

Reduction of 10b-Methyl-1,3,4,10b-tetrahydropyrimido[2,1-*a*]-isoindol-6(2H)-one (21b).—From 15.0 g (0.074 mol) of **26b**, 7.1 g (0.19 mol) of lithium aluminum hydride, and 600 ml of anhydrous diethyl ether (48 hr reflux) there was obtained 14.7 g of oil. Distillation (nitrogen) gave 11.4 g (82%) of 1-methyl-2-(3-aminopropyl)isoindole (**22b**): bp 138° (0.5 mm); $n^{20}D$ 1.6130; uv maxima 227 mμ (ε 43,640), 269 (2005), 280 (1585), 342 (3940); nmr ($CDCl_3$) δ 1.15 (2 H, D_2O exchangeable, NH_2), 1.78 (2 H, quintet, J = 7 cps, $\geqslant CCH_2C\leqslant$), 2.50 (3 H, s, CH_3), 2.47 (2 H, t, J = 7 cps, $CH_2N<$), 3.91 (2 H, t, J = 7 cps, $CH_2NC=$), 7.01 (1 H, s, CH=N), 6.87 (2 H), and 7.48 (2 H, A_2B_2, $(CHCH)_2$).

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.6; H, 8.6; N, 14.9. Found: C, 76.3; H, 8.4; N, 14.7.

Reduction of 1,3,4,10b-Tetrahydropyrimido[2,1-*a*]isoindol-6(2H)-one (21c).—From 6.0 g (0.032 mol) of **21c**, 3.0 g (0.08 mol) of lithium aluminum hydride, and 500 ml of diethyl ether (65 hr reflux) there was obtained 5.1 g of water-white liquid. Distillation in a kugelrohr (100°, 0.5 mm) gave 4.8 g (86%) of 2-(3-aminopropyl)isoindole (**22c**): $n^{20}D$ 1.6160; R_f 0.2 ($CHCl_3$–CH_3OH 95:5); ir (CH_2Cl_2) 2.74, 2.96, and 3.05 (NH_2), 6.80, 7.34, 7.53, and 8.82 μ; uv maxima 224 mμ (ε 31,500), 266 (1590), 270 (1520), 277 (1740), 289 (1380), 327 (4200), and 340 infl (3225); nmr ($CDCl_3$) δ 1.05 (2 H, D_2O exchangeable, NH_2), 1.58 (2 H, quintet, J = 6.0 cps, CH_2), 2.31 (2 H, t, J = 6.0 cps, CH_2N), 3.83 (2 H, t, J = 6.0 cps, $CH_2NC=$), 6.85 (2 H, s, HCN=CH), 6.88, and 7.43 (4 H, A_2B_2 pattern, HC=CH=CH=CH).

Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.8; H, 8.1; N, 16.1. Found: C, 75.9; H, 8.5; N, 16.4.

Reduction of 11b-Phenyl-1,2,3,4,5,11b-hexahydro-7H[1,3]-diazepino[2,1-*a*]isoindol-7-one (21d).—From 8.0 g (0.029 mol) of **21d**, 5.0 g (0.13 mol) of lithium aluminum hydride, and 25 ml of diethyl ether (17 hr reflux) there was obtained 8.2 g of oil. Crystallization from diethyl ether–heptane gave 3.1 g of solid, mp 116–160°, that was not studied. Concentration of the mother liquor gave 2.6 g of 1-phenyl-1,2,3,4,5,6,7,8-octahydro-2,7-benzodiazecine (**23**): mp 110–115°; analytical sample mp 112–114° (diethyl ether–pentane (lit.[1c] mp 114–116°); nmr ($CDCl_3$) δ 1.72 (4 H, m, $-CCH_2CH_2C-$), 2.35 (1 H, m, NCH), 2.82 (2 H, m, NCH_2), 2.60 (2 H, D_2O exchangeable, NH), 3.52 (1 H, m, NCH), 3.72 (H_A), 4.00 (H_B, J = 13.0 cps, $ArCH_AH_BN$), 5.17 (1 H, s, ArCHAr'), 6.50–7.53 (9 H, m, C_6H_5 and C_6H_4).

A solution of 0.3 g of **23**, 5.0 ml of pyridine, and 1.5 ml of acetic anhydride was refluxed (8 hr). The solvent was removed *in vacuo* and the residue crystallized from isopropyl alcohol to give 0.215 g of 2,7-diacetyl-substituted **23**: mp 174–176°; ir (KBr) 5.95 μ (CON); nmr ($CDCl_3$) δ 1.62 (4 H, m, $\geqslant CCH_2CH_2C\leqslant$), 2.08 (3 H, s, CH_3CO), 2.13 (1 H, m, NCH), 2.18 (3,H,s, CH_3CO), 3.10 (2 H, m, CH_2N), 4.32 (1 H, m, CHN), 4.28 (H_A), 5.68 (H_B, J = 14 cps, $ArCH_AH_BN$), 6.38 (1 H, s, ArCHAr'), 6.70–7.68 (9 H, m, C_6H_5 and C_6H_4).

Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.4; H, 7.5; N, 8.0; O, 9.1. Found: C, 75.1; H, 7.8; N, 8.3; O, 9.2.

Reduction of 5-Methyl-5a-*p*-chlorophenyl-5,5a,10,12-tetrahydroisoindolo[1,2-*b*]quinazoline-10,12-dione (24).—From 10.0 g (0.028 mol) of **24**, 5.2 g (0.14 mol) of lithium aluminum hydride, and 500 ml of anhydrous tetrahydrofuran (50 hr reflux) there was obtained 8.9 g of 5-methyl-5a-*p*-chlorophenyl-5,5a,10,12-tetrahydroisoindolo[1,2-*b*]quinazoline (**25**) as a yellow oil: R_f 0.92 ($CHCl_3$–CH_3OH 98:2); nmr ($CDCl_3$) δ 2.67 (3 H, s, NCH_3), 3.62 (H_A) and 4.07 (2 H, J = 17.0 cps, CH_AH_BN), 4.02 (2 H, s, CH_2N), and 6.40–7.35 (12 H, m, aromatic protons). Crystallization of 32 (8.5 g) from methanol–methylene chloride gave 6.8 g of 1-*p*-chlorophenyl-2-(*o*-methylaminobenzyl)isoindole (**26**): mp 206–208°; R_f 0.85 ($CHCl_3$–CH_3OH 98:2); ir (CH_2Cl_2) 2.72 and 2.91 (NH), 6.22, 6.30, 6.58, 6.67, 8.66, 9.14 and 9.90 μ; uv maxima 245 mμ sh (ε 19,500), 276 (6500), 287 (6500), 351 (6750), and 367 sh (1167); nmr ($CDCl_3$) δ 2.68 (3 H, s, NCH_3), 3.12 (1 H, broad, D_2O exchangeable, NH), 5.21 (2 H, s, NCH_2), 7.12 (1 H, s, C=CHN), and 6.51–7.67 (12 H, m, aromatic protons).

Anal. Calcd for $C_{22}H_{19}ClN_2$: C, 76.2; H, 5.5; Cl, 10.3; N, 8.0. Found: C, 76.4; H, 5.8; Cl, 10.0; N, 8.3.

Registry No.—Lithium aluminum hydride, 1302-30-3; **5b**, 17494-24-5; **6a**, 18409-76-2; **6b**, 19543-17-0; **6b** acetate, 19543-18-1; **6c**, 19543-19-2; **7**, 19543-20-5; **10**, 19543-21-6; **12**, 19543-22-7; **13b**, 5983-38-0; **13c**, 5983-39-1; **13d**, 5983-34-6; **13e**, 19553-20-9; **15a**, 19543-26-1; **15b**, 19104-44-0; **15c**, 19543-27-2; **15d**, 19581-60-3; **16a**, 19543-29-4; **19**, 19543-30-7; **20**, 19543-31-8; **21a**, 5965-49-8; **22a**, 19543-33-0; **22a** HCl, 19104-42-8; **22b**, 19543-35-2; **22c**, 19543-36-3; **23** (2,7-diacetyl), 19543-37-4; **24**, 19543-38-5; **25**, 19543-39-6; **26**, 19543-40-9; 1-methyl-2-(acetamidoethyl)isoindoline, 19543-28-3.

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