Synthesis of 1,2-Dihydroindolo[1,7-*ab*][1,5]benzodiazepines and Related Structures (1). A New Heterocyclic Ring System

Edward J. Glamkowski and James M. Fortunato*

Chemical Research Department, Hoechst-Roussel Pharmaceuticals Inc., Somerville, New Jersey 08876

Received January 15, 1979

The synthesis of the novel 1,2-dihydroindolo[1,7-*ab*][1,5]benzodiazepine ring system **4** is described. Condensation of 2-fluoronitrobenzene with indoline provided the starting material for the synthesis, 1-(2-nitrophenyl)indoline (**1a**) in high yield. The nitro group was reduced catalytically and the resulting amino function was acylated to afford the heterocycle percursor amide **3**. Refluxing this amide in phosphorus oxychloride brought about a Bischler-Napieralski type cyclodehydration to form the target 1,2-dihydroindolo[1,7-*ab*][1,5]benzodiazepine ring system. Dehydrogenation of the latter led to the fully aromatic indolo[1,7-*ab*][1,5]benzodiazepine structure **5**, while reduction with sodium borohydride provided the 1,2,6,7-tetrahydroindolo[1,7-*ab*]-[1,5]benzodiazepine tetracycle **6**.

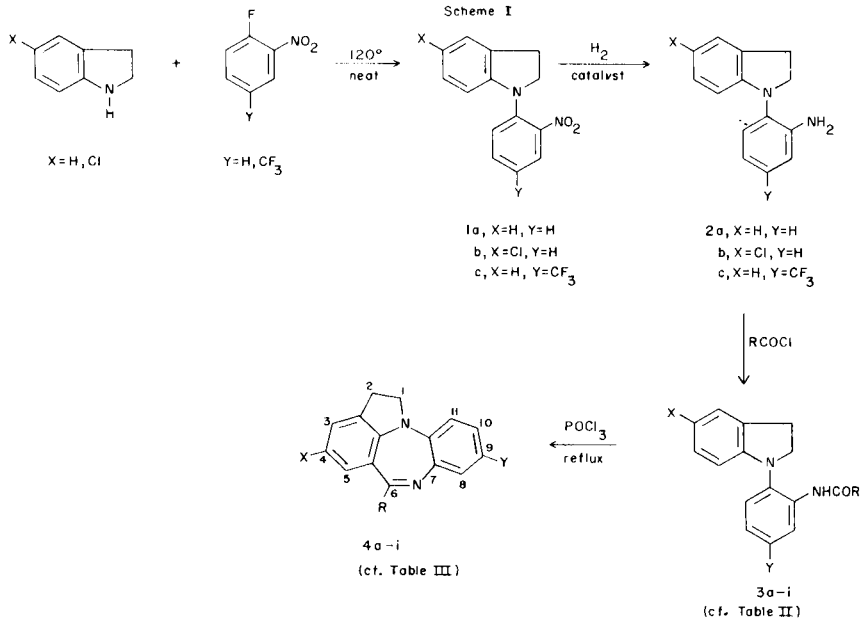
J. Heterocyclic Chem., **16**, 865 (1979).

Several years ago, we began a program using the Bischler-Napieralski cyclization reaction (2) to design novel heterocyclic ring systems. It was hoped that the resulting compounds would serve as a nucleus for derivatives of potential pharmacological interest. In connection with this program, we wish to report our initial synthetic studies which have led to the novel 1,2-dihydroindolo[1,7-*ab*][1,5]benzodiazepine ring system **4**. Dehydrogenation or reduction of this parent structure also provided the indolo **5** and tetrahydroindolo[1,7-*ab*][1,5]-benzodiazepines **6**, respectively.

The starting material required for the synthesis shown in Scheme I was 1-(2-nitrophenyl)indoline (**1a**). This was prepared in high yield by heating together neat, at 120°, 2-fluoronitrobenzene with two equivalents of indoline. Under these conditions, the nitrogen atom of indoline was sufficiently nucleophilic to displace fluoride from the highly activated nitrobenzene substrate. The excess indoline acted as the acceptor base for the hydrogen fluoride generated by the condensation. To provide tetracycles with a substituent in the six-membered rings, 5-chloroindoline (3) was reacted in the same manner to produce **1b**, while condensation of indoline with 4-chloro-3-nitrobenzotrifluoride furnished the starting material **1c**.

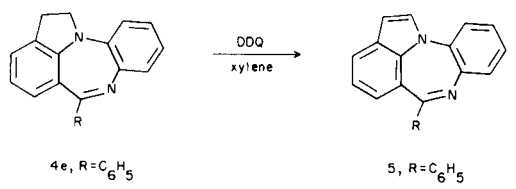
The nitro group in **1a-c** was reduced catalytically to afford the 1-(2-aminophenyl)indolines of type **2**. Nuclear chlorine was retained during the hydrogenation of **1b** by using 1% platinum-on-carbon as catalyst. In the next step, the amino group was acylated to provide the amide precursors **3** to the Bischler-Napieralski cyclization. When

Scheme I

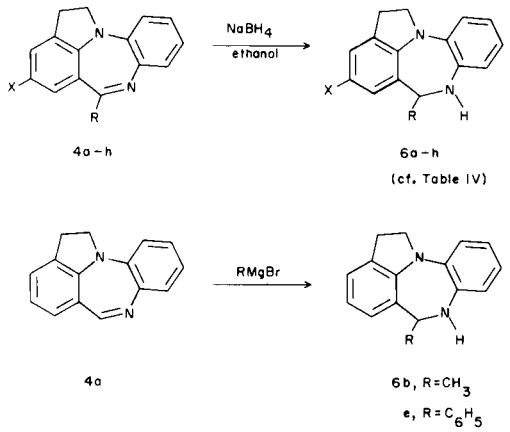


0022-152X/79/050865-05$02.25

Scheme II



Scheme III



these amides were refluxed in phosphorus oxychloride, cyclodehydration took place leading to the construction of a seven-membered central ring, and the novel 1,2-dihydroindolo[1,7-*ab*][1,5]benzodiazepines of formula **4**.

The nature of the pendant substituent R at position 6 in the tetracycle can be varied widely according to which acylating agent is chosen to form the precursor amide. By way of illustration, five different amides (Table II), with R groups ranging from hydrogen, alkyl, cycloalkyl and phenyl, were cyclized with approximately equal ease to the target tetracycles. This demonstrates the generality of the reaction, and the variety of pendant substituents which may be introduced (Table III). The cyclization was also unaffected by the presence of a chlorine atom in the indoline portion of the amide to give **4f-h**, or a trifluoromethyl group in the phenyl ring which led to **4i**.

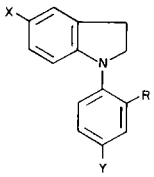
A fully aromatic tetracycle, 6-phenylindolo[1,7-*ab*][1,5]-benzodiazepine (**5**), was prepared by dehydrogenation of **4e** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), as shown in Scheme II.

The imino linkage in the central ring was reduced to provide a third class of tetracycles with the same skeletal framework, namely, the 1,2,6,7-tetrahydroindolo[1,7-*ab*]-[1,5]benzodiazepines of structure type **6** (Table IV). This was achieved smoothly and most conveniently with sodium borohydride (4) in ethanol (see Scheme III). It was also found that the imino linkage could, in effect, be reduced with concomitant introduction of a pendant group R by addition of a Grignard reagent to the polarized -C=N- of **4a**. Two examples are given in Scheme III. This provided an alternate synthesis of 6-substituted 1,2,6,7-tetrahydrotetracycles from a common precursor, **4a**. Several attempts were made to introduce a second methyl group at the -C(CH$_3$)=N- linkage of **4b**. However, under a variety of conditions, neither the methyl Grignard reagent, nor methyl lithium could be forced to add to the already substituted imino moiety.

The structures of the novel heterocycles of type **4**, **5**,

Table I

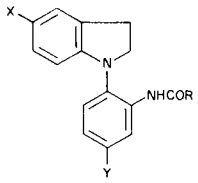
1-(2-Nitrophenyl)indolines (**1a-c**) and 1-(2-Aminophenyl)indolines (**2a-c**)



Compound	X	Y	R	M.p. °C	Yield %	Recrystallization Solvent	Molecular Formula	Analyses % Calcd. / Found		
1a	H	H	NO_2	62-64	84	isopropyl ether	$C_{14}H_{12}N_2O_2$	C, 69.99;	H, 5.03;	N, 11.66
								C, 70.08;	H, 5.13;	N, 11.93
1b	Cl	H	NO_2	89-91	27	isopropyl ether	$C_{14}H_{11}ClN_2O_2$	C, 61.21;	H, 4.04;	N, 10.20
								C, 61.10;	H, 4.13;	N, 10.19
1c	H	CF_3	NO_2	90-92	70	hexane	$C_{15}H_{11}F_3N_2O_2$	C, 58.43;	H, 3.60;	N, 9.09
								C, 57.98;	H, 3.58;	N, 9.18
2a	H	H	NH_2	233-236	74	methanol-ether	$C_{14}H_{14}N_2 \cdot HCl$	C, 68.15;	H, 6.13;	N, 11.35
								C, 67.93;	H, 6.04;	N, 11.35
2b	Cl	H	NH_2	235-238	32	methanol-ether	$C_{14}H_{13}ClN_2 \cdot HCl$	C, 59.80;	H, 5.03;	N, 9.96
								C, 59.88;	H, 5.15;	N, 9.98
2c	H	CF_3	NH_2	194-196	43	ethanol-ether	$C_{15}H_{13}F_3N_2 \cdot HCl$	C, 57.24;	H, 4.48;	Cl, 11.26
								C, 57.15;	H, 4.46;	Cl, 11.29

Table II

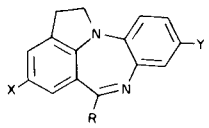
1-(2-Acylaminophenyl)indolines



Compound	X	Y	R	M.p.°C	Yield %	Recrystallization Solvent	Molecular Formula	Analyses % Calcd./Found		
3a	H	H	H	104-106	58	benzene-hexane	$C_{15}H_{14}N_2O$	C, 75.61;	H, 5.92;	N, 11.76
								C, 75.73;	H, 6.07;	N, 11.75
3b	H	H	CH_3	127-130	75	methanol	$C_{16}H_{16}N_2O$	C, 76.16;	H, 6.39;	N, 11.10
								C, 76.10;	H, 6.31;	N, 11.15
3c	H	H	$CH_2CH_2C_6H_5$	75-77	35	ether-hexane	$C_{23}H_{22}N_2O$	C, 80.67;	H, 6.48;	N, 8.18
								C, 80.78;	H, 6.52;	N, 8.28
3d	H	H	C_6H_{11}	87-89	62	ether-hexane	$C_{21}H_{24}N_2O$	C, 78.72;	H, 7.55;	N, 8.74
								C, 78.67;	H, 7.45;	N, 8.63
3e	H	H	C_6H_5	73-76	92	ethanol	$C_{21}H_{18}N_2O$	C, 80.23;	H, 5.77;	N, 8.91
								C, 80.15;	H, 5.80;	N, 8.91
3f	Cl	H	H	129-131	35	ethanol	$C_{15}H_{13}ClN_2O$	C, 66.06;	H, 4.80;	N, 10.27
								C, 66.25;	H, 4.92;	N, 10.40
3g	Cl	H	CH_3	144-145	69	toluene-isopropyl ether	$C_{16}H_{15}ClN_2O$	C, 67.02;	H, 5.27;	N, 9.77
								C, 66.94;	H, 5.30;	N, 9.75
3h	Cl	H	C_6H_5	44-46	72	ether-hexane	$C_{21}H_{17}ClN_2O$	C, 72.31;	H, 4.91;	N, 8.03
								C, 72.04;	H, 4.95;	N, 7.88
3i	H	CF_3	CH_3	153-155	41	ethanol	$C_{17}H_{15}F_3N_2O$	C, 63.75;	H, 4.72;	N, 8.75
								C, 63.75;	H, 4.71;	N, 8.89

Table III

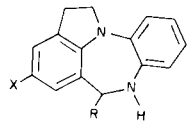
1,2-Dihydroindolo[1,7-*ab*][1,5]benzodiazepines



Compound	X	Y	R	M.p. °C	Yield %	Recrystallization Solvent	Molecular Formula	Analyses % Calcd./Found		
4a	H	H	H	231-232	72	acetic acid	$C_{15}H_{12}N_2 \cdot HCl$	C, 70.18;	H, 5.10;	N, 10.91
								C, 70.16;	H, 5.18;	N, 10.84
4b	H	H	CH_3	248-249	75	acetic acid-ethanol	$C_{16}H_{14}N_2 \cdot HCl$	C, 70.98;	H, 5.58;	Cl, 13.09
								C, 70.89;	H, 5.54;	Cl, 12.92
4c	H	H	$CH_2CH_2C_6H_5$	181-183	90	n-butanol	$C_{23}H_{20}N_2 \cdot HCl$	C, 76.55;	H, 5.86;	N, 7.76
								C, 76.57;	H, 5.90;	N, 7.85
4d	H	H	C_6H_{11}	104-106	24	ethanol-water	$C_{21}H_{22}N_2$	C, 83.40;	H, 7.33	
								C, 83.30;	H, 7.31	
4e	H	H	C_6H_5	141-143	29	ethanol	$C_{21}H_{16}N_2$	C, 85.10;	H, 5.44	
								C, 84.99;	H, 5.50	
4f	Cl	H	H	231-233	57	ethanol	$C_{15}H_{11}ClN_2 \cdot HCl$	C, 61.87;	H, 4.15;	N, 9.62
								C, 61.73;	H, 4.08;	N, 9.47
4g	Cl	H	CH_3	251-254	26	acetic acid-ethanol	$C_{16}H_{13}ClN_2 \cdot HCl$	C, 62.97;	H, 4.62;	Cl, 23.23
								C, 63.26;	H, 4.54;	Cl, 22.65
4h	Cl	H	C_6H_5	231 dec.	29	ethanol	$C_{21}H_{15}ClN_2 \cdot HCl$	C, 68.68;	H, 4.39;	Cl, 19.30
								C, 68.41;	H, 4.44;	Cl, 18.95
4i	H	CF_3	CH_3	240-242	37	ethanol	$C_{17}H_{13}F_3N_2 \cdot HCl$	C, 60.28;	H, 4.17;	N, 8.27
								C, 60.13;	H, 4.20;	N, 8.33

Table IV

1,2,6,7-Tetrahydroindolo[1,7-*ab*][1,5]benzodiazepines



Compound	X	R	M.p. °C	Yield %	Recrystallization Solvent	Molecular Formula	Analyses % Calcd./Found		
6a	H	H	175-177	56	benzene	$C_{15}H_{14}N_2$	C, 81.05;	H, 6.35	
							C, 81.13;	H, 6.41	
6b	H	CH_3	134-136	69	benzene	$C_{16}H_{16}N_2$	C, 81.32;	H, 6.82	
							C, 81.17;	H, 6.84	
6c	H	$CH_2CH_2C_6H_5$	191-193	87	ether	$C_{23}H_{22}N_2 0.5C_2H_2O_4$	C, 77.81;	H, 5.98;	N, 7.56
							C, 78.14;	H, 6.08;	N, 7.74
6d	H	C_6H_{11}	136-138	40	ether-heptane	$C_{21}H_{24}N_2$	C, 82.85;	H, 7.95	
							C, 82.74;	H, 7.98	
6e	H	C_6H_5	161-164	46	2-propanol	$C_{21}H_{18}N_2$	C, 84.53;	H, 6.08	
							C, 84.45;	H, 6.00	
6f	Cl	H	248-251	42	ethanol	$C_{15}H_{13}ClN_2 \cdot HCl$	C, 61.45;	H, 4.81;	N, 9.55
							C, 61.56;	H, 5.05;	N, 9.77
6g	Cl	CH_3	167-170	45	toluene	$C_{16}H_{15}ClN_2$	C, 70.98;	H, 5.58;	N, 10.35
							C, 71.10;	H, 5.31;	N, 10.29
6h	Cl	C_6H_5	192-194	73	chloroform-ether	$C_{21}H_{17}ClN_2$	C, 75.78;	H, 5.15;	Cl, 10.65
							C, 75.80;	H, 5.23;	Cl, 10.79

and **6** were confirmed by elemental analyses, and their ir, nmr and mass spectra.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 457 grating spectrophotometer. Nuclear magnetic resonance spectra were taken on a Jeol C-60HL instrument. Chemical shifts are reported as δ units with tetramethylsilane as an internal standard. The mass spectra were obtained from a Finnigan Model 4000 spectrophotometer with an INCOS data system at 70 eV by direct insertion. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

The yields reported in Tables I-IV represent analytically pure products. No attempt was made to optimize yields.

1-(2-Nitrophenyl)indoline (**1a**).

A stirred solution, kept under nitrogen, of 423 g. (3.55 moles) of indoline and 212 g. (1.50 moles) of 1-fluoro-2-nitrobenzene was heated at 120° overnight. The resulting mixture was then cooled and partitioned between chloroform and water. The organic phase was separated and extracted twice with 3*N* hydrochloric acid, and once with water. After drying over anhydrous sodium sulfate, the solvent was removed *in vacuo* to leave 296 g. of oil. This was dissolved in 700 ml. of hot isopropyl ether from which 228 g. (84% yield) of pure **1a** (Table I) separated as orange-red crystals; ir (potassium bromide): 1590 (aromatic C=C), 1485 and 1335 (Ar-NO_2), 1285 cm^{-1}; nmr (DMSO-d_6): δ 3.11 (t, 2H, CH_2), 3.89 (t, 2H, CH_2), 6.30-8.12 (m, 8H, ArH).

Compound **1b** was prepared in a similar manner and its properties are reported in Table I.

1-(2-Nitro-4-trifluoromethylphenyl)indoline (**1c**).

An initial solution of 59.6 g. (0.50 mole) of indoline and 45.2 g. (0.20 mole) of 4-chloro-3-nitrobenzotrifluoride in 500 ml. of xylene was stirred and refluxed under nitrogen overnight. The indoline hydrochloride salt which had separated was then filtered off. The xylene filtrate was extracted twice with 3*N* hydrochloric acid, once with 3*N* sodium hydroxide, once with water, dried over anhydrous magnesium sulfate, and finally concentrated to a stiff oil weighing 58 g. This was dissolved in 300 ml. of hot hexane to afford 42.9 g. (70% yield) of pure **1c** (Table I) in the form of orange-red prisms; ir (potassium bromide): 1648 (aromatic C=C), 1530 and 1390 (Ar-NO_2), 1325 cm^{-1}; nmr (DMSO-d_6): δ 3.30 (t, 2H, CH_2), 4.15 (t, 2H, CH_2), 6.90-7.78 (m, 4H, Ar-H), 8.28-8.35 (m, 2H, Ar-H), 8.75 (broad s, 1H, Ar-H).

1-(2-Aminophenyl)indoline Hydrochloride (**2a**).

A solution of 24.0 g. (0.10 mole) of **1a** in 400 ml. of ethanol and 40 ml. of benzene was shaken with 2.5 g. of 5% palladium-on-carbon at 60 psi of hydrogen until the theoretical amount of hydrogen was taken up. The catalyst was then removed by filtration and the filtrate was concentrated to an oil. This was dissolved in 150 ml. of ether, cooled to 0°, and treated with gaseous hydrogen chloride to precipitate 23.5 g. (95%) of off-white crystals, m.p. 230-236°. Purification was accomplished by dissolving the salt in 200 ml. of methanol without heating and then adding 400 ml. of ether. This furnished 18.0 g. (74% overall yield) of fluffy white crystals of pure **2a** (Table I), m.p. 233-236°; ir (potassium bromide): 3440 (broad) and 3055-2650 (Ar-NH_3^+), 1600 (aromatic C=C), 1480, 750 cm^{-1}; nmr (DMSO-d_6): δ 3.33 (t, 2H, CH_2), 4.03 (t, 2H, CH_2), 6.58-8.35 (m, 8H, Ar-H), 8.77 (broad s, 3H, Ar-NH_3^+).

Amines **2b** (but using 1% platinum-on-carbon to retain nuclear chlorine) and **2c** were prepared in the same manner. Their properties are described in Table I.

1-(2-Formamidophenyl)indoline (**3a**).

A stirred mixture of 24.7 g. (0.10 mole) of **2a** in 150 ml. of dimethylformamide was immersed in an oil bath preheated to 100°. Then 16.2 g. (0.30 mole) of sodium methoxide was added in one portion. The mixture was rapidly brought to reflux and kept at reflux for 1 hour. Then 300 ml. of water was added to precipitate the product. After stirring for 1 hour at

ambient temperature, the amide was collected, washed well with water and dried. The crude solid was dissolved in 250 ml. of benzene (charcoal) and the solution was diluted with 1250 ml. of hexane. This provided 13.7 g. (58% yield) of fluffy white crystals of pure **3a** (Table II); ir (potassium bromide): 3200 (NH), 1680 (C=O), 1660, 1530, 1458 cm^{-1}; nmr (DMSO-d_6): δ 3.28 (t, 2H, CH_2), 3.92 (t, 2H, CH_2), 6.45 (d, 1H, CHO), 6.90-7.84 (m, 6H, Ar-H), 8.82 (m, 2H, Ar-H), 9.75 (broad, s, 1H, NH).

The chloroformamide **3f** (Table II) was prepared in the same way.

1-(2-Acetamidophenyl)indoline (**3b**).

A stirred slurry, under nitrogen, of 9.96 g. (0.04 mole) of **2a** in 100 ml. of dichloromethane was treated with 10.1 g. (0.10 mole) of triethylamine over a 15 minute period. The nature of the mixture changed as the free base of **2a** passed into solution and triethylamine hydrochloride precipitated out. After cooling to 0-5°, 4.7 g. (0.06 mole) of acetyl chloride was added dropwise over 0.5 hour. The mixture was stirred overnight, and then 100 ml. of water was added to dissolve the salt. The organic phase was separated, washed with 3*N* hydrochloric acid, 3*N* sodium hydroxide, with water, then dried over anhydrous magnesium sulfate, and concentrated. This left a crystalline residue weighing 9.2 g. with m.p. 125-128°. Recrystallization from 50 ml. of methanol (charcoal) gave 7.5 g. (75% yield) of pure **3b** (Table II) as colorless needles, m.p. 127-130°; ir (potassium bromide): 3320 (NH), 1670 (C=O), 1590, 1510, 1442 cm^{-1}; nmr (DMSO-d_6): δ 2.10 (s, 3H, CH_3), 3.25 (t, 2H, CH_2), 3.93 (t, 2H, CH_2), 6.48 (d, 1H, Ar-H), 6.84-7.80 (m, 6H, Ar-H), 8.30-8.48 (m, 1H, Ar-H), 9.14 (broad s, 1H, NH).

Similarly prepared were amides **3c-e** and **3g-i** of Table II.

1,2-Dihydroindolo[1,7-*ab*][1,5]benzodiazepine Hydrochloride (**4a**).

A mixture of 14.0 g. (0.058 mole) of **3a** and 50 ml. of phosphorus oxychloride was stirred and refluxed under nitrogen overnight. Excess phosphorus oxychloride was then removed, first at aspirator pressure with mild heating, and finally *in vacuo*. This left a soft dark solid (22 g.) which was triturated and boiled with 50 ml. of absolute ethanol. This mixture was stirred 1 hour to homogenize the fine, purple colored solid, then it was filtered, washed twice with ethanol, twice with ether, and dried to afford 10.9 g. (72%) of virtually pure microcrystalline **4a**, m.p. 228-230°. An analytical sample was recrystallized from acetic acid as tiny purple needles and had m.p. 231-232° (Table III); ir (nujol): 2490 (=NH^+), 1658, 1615 (C=N, aromatic C=C), 1460, 735, 720 cm^{-1}; nmr (deuterotrifluoroacetic acid): δ 2.85 (t, 2H, CH_2), 3.48 (t, 2H, CH_2), 6.25-7.30 (m, 8H, Ar-H); ms: m/e 220 (M^+ of the base).

The procedure described above was employed to prepare the tetracycles **4b-c** and **4f-i** of Table III.

In two cases, **4d** and **4e**, the tetracycle could not be easily purified by recrystallization of the hydrochloride salt which was formed **in situ** and isolated directly from the cyclization reaction. These were therefore converted to the free base and purified as such, as illustrated in the following example.

6-Cyclohexyl-1,2-dihydroindolo[1,7-*ab*][1,5]benzodiazepine (**4d**).

A solution of 12.1 g. (0.037 mole) of amide **3d** in 50 ml. of phosphorus oxychloride was stirred and refluxed under nitrogen overnight. The excess phosphorus oxychloride was then removed first at aspirator pressure, and finally *in vacuo*. This left the product as a purple syrup. This was dissolved in 75 ml. of absolute ethanol and treated with an excess of tri-*n*-butylamine. The resulting solution was partitioned between ether and water. The ether phase was separated, washed again with water, twice with brine, then dried over anhydrous potassium carbonate and concentrated to give 13.8 g. Recrystallization from ethanol-water afforded 4.76 g. (24% yield) of pure yellow crystals of **4d**; ir (potassium bromide): 1630, 1600 (C=N, aromatic C=C), 1475, 1450, 743 cm^{-1}; nmr (DMSO-d_6): δ 1.05-2.10 (broad envelope, 11H, cyclohexyl CH, CH_2), 3.02 (t, 2H, CH_2), 3.85 (t, 2H, CH_2), 6.90-7.60 (m, 7H, Ar-H); ms: m/e 302 (M^+).

6-Phenylindolo[1,7-*ab*][1,5]benzodiazepine (**5**).

A stirred solution, under nitrogen, of 8.70 g. (0.0294 mole) of **4e** in 125 ml. of xylene was heated to 100° when 7.34 g. (0.0323 mole) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was added in one portion. The mixture was then refluxed for three hours. After cooling to room temperature, the supernatant liquid was decanted and filtered. The dark residue remaining in the flask was rinsed twice with 25 ml. of xylene. The xylene portions were combined and concentrated to 8.8 g. of oil. This was dissolved in 20 ml. of hot ethanol and the initial solution was kept at 0° overnight. The crystals so obtained were found to weigh 3.8 g., m.p. 128-136°. Recrystallization from 90 ml. of ethanol (charcoal) afforded 2.7 g. (31% yield) of pure **5** in the form of tiny orange-yellow needles, m.p. 136-138°; ir (chloroform): 1618 (aromatic C=C), 1520, 1480, 1415, 1320, 1250 cm^{-1}; nmr (DMSO-d_6): δ 6.68-8.50 (several overlapping m, 15H, Ar-H); ms: m/e 294 (M^+).

Anal. Calcd. for $C_{21}H_{14}N_2$: C, 85.69; H, 4.79. Found: C, 85.44; H, 4.82.

1,2,6,7-Tetrahydroindolo[1,7-*ab*][1,5]benzodiazepine (**6a**).

A stirred mixture, under nitrogen, of 18.0 g. (0.07 mole) of **4a** in 100 ml. of absolute ethanol was cooled to 0° and then sodium borohydride was added in small portions at such a rate as to minimize frothing and to keep the reaction temperature below 5°. The addition took 1 hour and 3 g. of borohydride was required to discharge the initial purple color of the imino compound, and another 0.5 g. was added to insure completeness of reduction. An hour later, 50 ml. of water was added in portions to decompose excess reagent and to maximize precipitation of the product. The crystalline solid was filtered, washed well with water, and dried to afford 15.1 g. (98%). Recrystallization twice from benzene provided 8.50 g. (56% yield) of white needles (Table IV); ir (chloroform): 3375 (NH), 1598 (aromatic C=C), 1515, 1480, 1460 cm^{-1}; nmr (DMSO-d_6): δ 3.10 (t, 2H, CH_2), 3.80-4.03 (overlapping d and t, 4H, CH_2, CH_2), 5.70 (broad, 1H, NH), 6.45-7.15 (m, 7H, Ar-H); ms: m/e 222 (M^+).

The other reduced tetracycles **6b-h** of Table IV were prepared in the same manner as above. Compounds **6c** and **6f** were purified as the oxalate and hydrochloride salts, respectively.

6-Methyl-1,2,6,7-tetrahydroindolo[1,7-*ab*][1,5]benzodiazepine (**6b**). Reaction of the Imino Linkage with a Grignard Reagent.

A slurry of 2.00 g. (0.0078 mole) of **4a** and 2.16 g. (0.0156 mole) of potassium carbonate in 50 ml. of tetrahydrofuran was stirred for 1 hour, then filtered. The filtrate, containing the tetracycle free base, was cooled to 0° under nitrogen and treated dropwise with 10 ml. of a 2.5 molar solution of methyl magnesium bromide in ether. The mixture was then stirred for 1 hour at room temperature followed by 1 hour at reflux. After cooling to 0°, a saturated solution of ammonium chloride was added cautiously to quench the reaction. The resulting mixture was partitioned between dichloromethane and water. The organic phase was separated and extracted with brine, then dried over anhydrous sodium sulfate and concentrated to a crystalline solid. Recrystallization from benzene afforded 1.24 g. (68% yield) of pure **6b**, m.p. 134-136°; ir (chloroform): 3360 (NH), 1592 (aromatic C=C), 1508, 1473, 1452 cm^{-1}; nmr (DMSO-d_6): δ 1.18 (d, 3H, CH_3), 3.08 (t, 2H, CH_2), 3.72-4.40 (overlapping t and m, 3H, CH_2, CH), 5.40 (broad, 1H, NH), 6.45-7.12 (m, 7H, Ar-H); ms: m/e 236 (M^+).

The Grignard addition of phenyl magnesium bromide to **4a** was carried out in the same manner as above to provide **6e** in 65% yield.

Acknowledgment.

The authors wish to thank Marc N. Agnew and David R. Claire, Jr. for determining the ir, nmr and mass spectra.

REFERENCES AND NOTES

(1) Presented in part at the 177th National American Chemical Society Meeting, Honolulu, Hawaii, April 1-6, 1979.

(2) W. M. Whaley and T. Govindachari, in "Organic Reactions", Vol. VI, R. Adams, Ed., John Wiley and Sons, Inc., New York, N. Y., 1967, p. 74.

(3) J. B. Hester, A. D. Rudzik and W. Veldkamp, *J. Med. Chem.*, **13**, 827 (1970).

(4) Borane in tetrahydrofuran, available from the Aldrich Chemical Company, Milwaukee, Wis., was also an effective reducing agent for the imino bond.