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3,4-Dihydro-1*H*-1,4-oxazino[4,3-*a*]indoles as Potential Antidepressants

Christopher A. Demerson, George Santroch, Leslie G. Humber,*

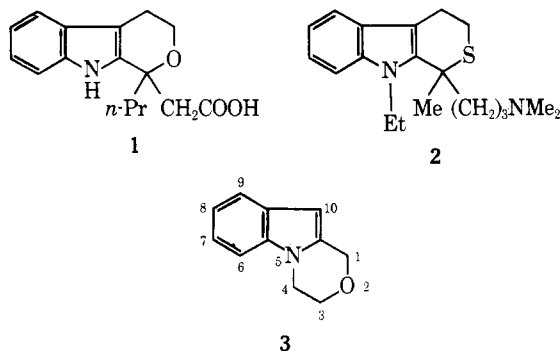
Department of Chemistry

and Marie-Paule Charest

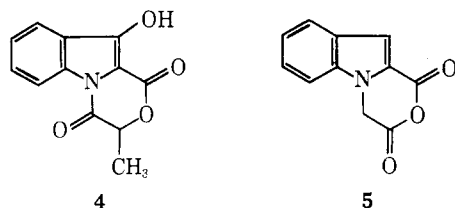
Department of Pharmacology, Ayerst Research Laboratories, Montreal, Canada. Received December 3, 1974

A series of 3,4-dihydro-1*H*-1,4-oxazino[4,3-*a*]indoles bearing basic side chains has been synthesized by a novel chemical process. These compounds have been screened for potential antidepressant activity. One of these derivatives, 3,4-dihydro-1,10-dimethyl-1-(3-methylaminopropyl)-1*H*-1,4-oxazino[4,3-*a*]indole (AY-23,673), was particularly potent in the prevention of reserpine ptosis test in mice, with an ED₅₀ of 0.5 mg/kg ip.

Recent reports from this laboratory have described novel synthetic routes to pyrano- and thiopyrano-fused indolic systems which have led to the development of prodolic acid[†] (1), an antiinflammatory agent,¹ and tandamine hydrochloride[†] (2), a potential antidepressant.² This report describes the synthesis and antidepressant properties of a series of compounds containing the 3,4-dihydro-1*H*-1,4-oxazino[4,3-*a*]indole system 3 and bearing basic side chains attached at position 1.



Chemistry. The only reported syntheses of oxazino[4,3-*a*]indoles are the preparation of 4 in 1949³ and of 5 in 1952.⁴ The synthetic routes used in those studies are not suitable for the synthesis of the types of derivatives described in this report. In the present investigation we have utilized a reaction whose potential for the formation of α,α -disubstituted pyrano rings was first recognized in our laboratory.⁵ It involves the acid-catalyzed intramolecular



alkylation of an aryl ring by a hemiketal formed in situ from an aryethanol and a carbonyl component. Its application to the synthesis of 1,1-disubstituted 3,4-dihydro-1*H*-

1,4-oxazino[4,3-*a*]indoles is illustrated in Scheme I. The 3-methyl- and 3-ethylindole-1-ethanols (6 and 7, respectively) were allowed to react with the appropriate keto ester in benzene with *p*-toluenesulfonic acid as catalyst, followed directly by hydrolysis, to afford the 1,10-dialkyl-1-alkanoic acids 8–12 which are described in detail in Table I. The required indole-1-ethanol 6 was obtained from the readily available 3-methylindole and ethylene oxide, while 7 was prepared from the reaction of 3-ethylindole⁶ with ethyl bromoacetate, followed by reduction of the resulting 1-acetic acid derivative with lithium aluminum hydride (see Experimental Section).

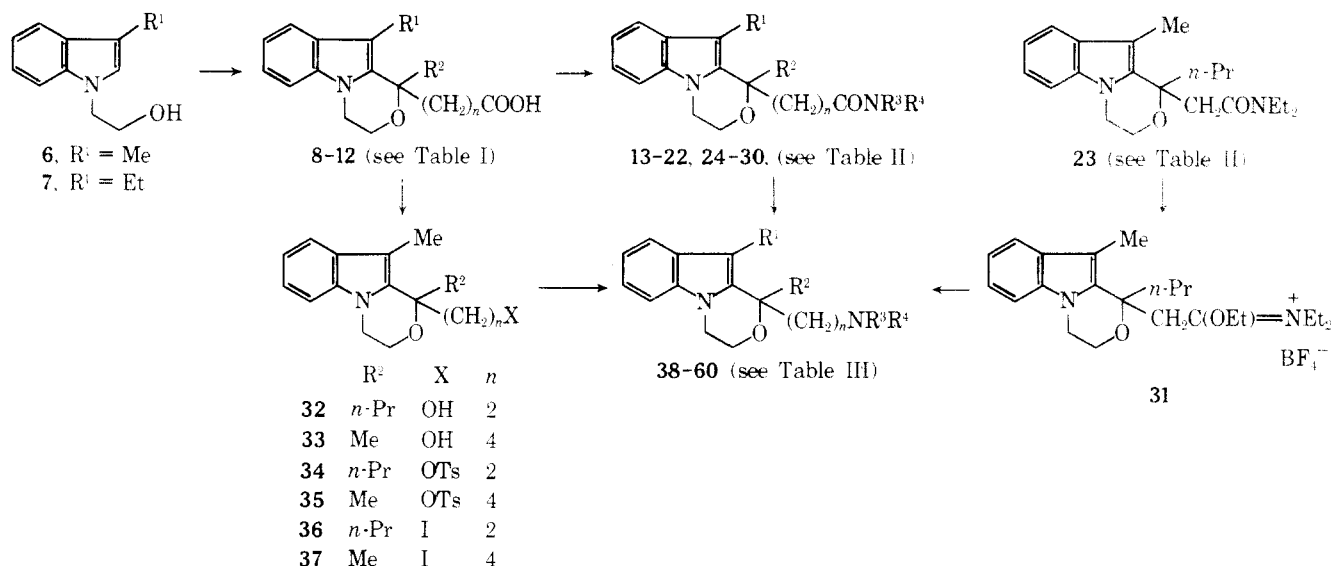
The five alkanolic acids 8–12 were ultimately transformed to the 23 basic derivatives 38–60 collected in Table III. Thus, the amides 13–30 were prepared from the corresponding alkanolic acids by conversion to the mixed anhydrides with ethyl chloroformate followed by reaction with the appropriate amine. The amides were reduced, either directly with lithium aluminum hydride (path A) or, in one case, via sodium borohydride reduction⁷ of the ethoxyiminium salt 31 derived from amide 23 with triethyloxonium fluoroborate. Some of the basic compounds were best prepared from the acids via the intermediate alcohols 32 and 33, tosylates 34 and 35, and iodides 36 and 37 (path B). The intermediates 32–37 were characterized by spectroscopy and, with the exception of 37, were obtained as oils. Reaction of these iodides with the appropriate amines afforded the required basic compounds.

Chemical data on the compounds referred to in Scheme I as well as definitions of the range of the variables R₁–R₄ and *n* are collected in Tables I–III and some detailed reaction conditions are given in the Experimental Section.

Pharmacology. The 23 compounds listed in Table III were investigated as antidepressant agents. The results are shown in Table III along with the activities of two standard antidepressants, amitriptyline (61) and imipramine (62). Acute toxicity was investigated ip in albino mice. Graded doses of the compounds were administered to groups of five animals each. The approximate LD₅₀ was determined from the 5-day mortality data. Prevention of reserpine-induced ptosis was estimated by an adaptation of the method of Petersen et al.⁸ The percentage of mice in which ptosis was prevented was recorded. The ED₅₀ was determined according to the method of Finney.⁹

[†] Nonproprietary names adopted by the USAN Council.

Scheme I



Five of the oxazinoindoles, 38, 43-45, and 54, were more active than amitriptyline in preventing reserpine ptosis, with 43 being the most active with an ED₅₀ of 0.5 mg/kg.

It is evident that the nature of the aminoalkyl side chain at position 1 of the ring system has a profound influence on the activity of the derivatives. Four side chains were found to impart the greatest activity, in the following order: methylaminopropyl > dimethylaminoethyl \approx dimethylaminopropyl > aminopropyl (43 > 38 \approx 45 > 44). Lengthening the side chain to 4 carbons as in 47-49 decreased the activity, as did increasing the bulk of the nitrogen substituent. Replacement of the methyl groups at positions 1 and 10 with *n*-propyl and ethyl groups also gave less active compounds (51 and 54).

In conclusion, the synthesis and pharmacological testing of a series of 23 novel oxazinoindole derivatives has led to the identification of 43, 3,4-dihydro-1,10-dimethyl-1-methylaminopropyl-1*H*-1,4-oxazino[4,3-*a*]indole hydrochloride,[†] as a potential antidepressant agent on the basis of its activity in preventing reserpine ptosis (ED₅₀ 0.5 mg/kg). Further studies on the biological profile of this compound will be reported separately.

Experimental Section

Melting points were taken on a Thomas-Hoover apparatus and need no correction. NMR spectra were determined using a Varian A-60A spectrometer and the chemical shifts (δ) are reported in parts per million downfield from TMS. Analyses indicated by elemental symbols were within $\pm 0.4\%$ of the theoretical values and were done by Dr. G. Schilling and staff of our laboratories on a Perkin-Elmer Model 240 elemental analyzer.

3-Methylindole-1-ethanol (6). 3-Methylindole (393 g, 3 mol) in 1000 ml of dry THF was added dropwise with cooling to *n*-butyllithium (3.05 mol) in 1000 ml of THF. The reaction mixture was stirred for 1 hr at 0° and then ethylene oxide (300 ml, 6 mol) in 300 ml of dry THF was added. The reaction temperature was raised to 22° and stirring was continued for 18 hr. Most of the THF was evaporated off and the residue taken into CH₂Cl₂, washed with concentrated HCl, 10% NaHCO₃, and H₂O, dried over Na₂SO₄, and distilled to afford the product (86%): bp 120-125° (0.1 mm). Anal. (C₁₁H₁₃NO) C, H, N.

3-Ethylindole-1-ethanol (7). 3-Ethylindole (25 g, 0.173 mol) in 300 ml of DMF was added dropwise to a stirring mixture of NaH (10.0 g of a 55% oil dispersion, 0.23 mol) in 325 ml of DMF. This was heated at 40° for 2 hr. After cooling to 0° ethyl bromoacetate (57 g, 0.34 mol) was added dropwise while keeping the reaction temperature under 20°. After the addition, stirring was continued

for 90 min. H₂O was added dropwise to destroy excess sodium hydride. A conventional work-up procedure afforded the crude ester which was hydrolyzed directly with KOH in aqueous MeOH at 22° to 3-ethylindole-1-acetic acid (25 g, 71%): mp 157-159° (MeOH); NMR (CDCl₃) δ 1.21 (t, 3, *J* = 7 Hz, CH₃), 1.33 (t, 3, *J* = 7 Hz, CH₃), 2.78 (q, 2, *J* = 7 Hz, CH₂CH₃), 4.18 (q, 2, *J* = 7 Hz, OCH₂CH₃), 4.72 (s, 2, CH₂CO), 6.84 (s, 1, =CH), 7.20-7.60 (m, 4, aromatic). Anal. (C₁₂H₁₃NO₂) C, H, N.

This acid (20 g, 0.1 mol) in 500 ml of Et₂O was slowly added to a stirring mixture of LiAlH₄ (4.6 g, 0.12 mol) in 350 ml of Et₂O at 15° and the reaction was stirred for 15 min at this temperature. The usual work-up procedure afforded an oil which was purified by chromatography on silica gel with 15% EtOAc in C₆H₆. The product was obtained as an oil (15.5 g, 82%): NMR (CDCl₃) δ 1.3 (t, 3, *J* = 7 Hz, CH₃), 1.85 (s, 1, OH), 2.77 (q, 2, *J* = 7 Hz, CH₂CH₃), 3.68 (t, 2, *J* = 5 Hz, CH₂N), 4.02 (t, 2, *J* = 5 Hz, CH₂O), 6.82 (m, 1, CH), 6.9-7.7 (m, 4, aromatic).

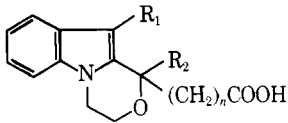
Preparation of the Alkanoids 8-12 (Table I). 3,4-Dihydro-1,10-dimethyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-acetic Acid (8). A mixture of 3-methylindole-1-ethanol (6, 26.5 g, 0.15 mol), ethyl acetoacetate (32 g, 0.20 mol), and *p*-toluenesulfonic acid (2.0 g) in 600 ml of C₆H₆ was refluxed 6 hr under a Dean-Stark water trap. The reaction solution was washed with 5% NaHCO₃ and H₂O, dried over Na₂SO₄, and evaporated to give the ester as an oil which was purified by chromatography on silica gel with 10% EtOAc in C₆H₆. The crude ester was dissolved in 800 ml of MeOH containing 20 g of KOH and 20 ml of H₂O and heated at 50° for 2 hr. A conventional work-up procedure afforded the product 8 (25 g, 65%): mp 138-139°.

In an analogous manner the alkanoids 9-12 were prepared using the appropriate starting materials. Chemical data on these compounds are collected in Table I.

Preparation of the Amides 13-30 (Table II). 3,4-Dihydro-*N*-ethyl-1,10-dimethyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-acetamide (15). A stirred solution of the acid 8 (10 g, 0.039 mol) and triethylamine (6 g, 0.039 mol) in 150 ml of THF was cooled to -5°. Ethyl chloroformate (5 g, 0.046 mol) was added dropwise and stirring continued for 2 hr while keeping the temperature below 10°. The mixture was cooled to -10° and treated with ethylamine (75 ml of a 35% aqueous solution, 0.58 mol). After 1 hr, most of the THF was evaporated off and the residue partitioned between Et₂O and H₂O. The ethereal solution was dried over Na₂SO₄ and concentrated in vacuo to afford the amide 15 (11 g, 98%): mp 104-106°. Similarly, amides 13, 14, and 16-30 were prepared from the appropriate acids of Table I and the appropriate commercially available amines. Chemical data on these compounds are collected in Table II.

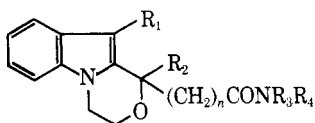
Preparation of the Amines 38-60. Path A. LiAlH₄ Reduction of Amides 13-22 and 24-30. 3,4-Dihydro-1-[(2-dimethylamino)ethyl]-1,10-dimethyl-1*H*-1,4-oxazino[4,3-*a*]indole (38). The amide 13 (11 g, 0.038 mol) was reduced in THF (200 ml) with LiAlH₄ (6.3 g, 0.16 mol) during 2 hr at reflux. A conventional work-up gave the product (8 g, 77%) as an oil. It was converted directly to the HCl salt which had mp 237-239°.

[†] Also known by the Ayerst code number, AY-23,673.

Table I. 3,4-Dihydro-1,10-dialkyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-alkanoic Acids


No. ^a	R ₁	R ₂	<i>n</i>	Reflux time, hr ^b	Mp, °C	Recrystn solvent ^c	Yield, % ^d	Formula ^e
8	CH ₃	CH ₃	1	48	138–139	A	65	C ₁₅ H ₁₇ NO ₃
9	CH ₃	CH ₃	2	12	115–116	A, B	73	C ₁₆ H ₁₉ NO ₃
10	CH ₃	<i>n</i> -C ₃ H ₇	1	48	146–148	B	59	C ₁₇ H ₂₁ NO ₃
11	CH ₃	CH ₃	3	3.5	104–106	B	92	C ₁₇ H ₂₁ NO ₃
12	C ₂ H ₅	CH ₃	2	12	119–121	A, B	42	C ₁₇ H ₂₁ NO ₃

^aThe indole starting material was 3-methylindole-1-ethanol (6) except for compound 12 where 3-ethylindole-1-ethanol (7) was used. The keto esters used were ethyl acetoacetate for 8, ethyl levulinate for 9 and 12, ethyl butyrylacetate for 10, and ethyl δ -ketoheptanoate for 11. ^bReflux time required for cyclization. ^cA = petroleum ether (bp 40–60°); B = ethyl acetate. ^dThese are overall yields for the cyclization of the indoleethanol with the keto ester followed by saponification. ^eAll compounds analyzed for C, H, and N within $\pm 0.4\%$ of the calculated values.

Table II. *N*-Substituted 3,4-Dihydro-1,10-dialkyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-acetamides and -propionamides


No.	R ₁	R ₂	NR ₃ R ₄	<i>n</i>	Mp, °C	Recrystn solvent ^a	Yield, % ^b	Formula ^c (analyses)
13	Me	Me	NMe ₂	1	<i>d</i>			C ₁₇ H ₂₂ N ₂ O ₂
14	Me	Me	NHMe	1	131–133	A	86	C ₁₆ H ₂₀ N ₂ O ₂ (C, H, N)
15	Me	Me	NHEt	1	104–106	A	98	C ₁₇ H ₂₂ N ₂ O ₂ (C, H, N)
16	Me	Me	NEt ₂	1	<i>d</i>			C ₁₉ H ₂₆ N ₂ O ₂
17	Me	Me	NHMe	2	147–149	A	100	C ₁₇ H ₂₂ N ₂ O ₂ (C, H, N)
18	Me	Me	NH ₂	2	97–98	B, C	87	C ₁₆ H ₂₀ N ₂ O ₂ (C, H, N)
19	Me	Me	NMe ₂	2	<i>d</i>			C ₁₈ H ₂₄ N ₂ O ₂
20	Me	Me	NHEt	2	114–116	A, B	100	C ₁₈ H ₂₄ N ₂ O ₂ (C, H, N)
21	Me	Me	NEt ₂	2	<i>d</i>			C ₂₀ H ₂₈ N ₂ O ₂
22	Me	<i>n</i> -Pr	NMe ₂	1	84–86	A	67	C ₁₉ H ₂₆ N ₂ O ₂ (C, H, N)
23	Me	<i>n</i> -Pr	NEt ₂	1	<i>d</i>			C ₂₁ H ₃₀ N ₂ O ₂
24	Et	Me	NHMe	2	137–139	A	100	C ₁₈ H ₂₄ N ₂ O ₂ (C, H, N)
25	Me	Me	C ₅ H ₁₀ N ^e	1	<i>d</i>			C ₂₀ H ₂₆ N ₂ O ₂
26	Me	Me	C ₅ H ₁₁ N ₂ ^e	1	<i>d</i>			C ₂₀ H ₂₇ N ₃ O ₂
27	Me	Me	C ₄ H ₈ NO ^e	1	<i>d</i>			C ₁₉ H ₂₄ N ₂ O ₃
28	Me	Me	C ₅ H ₁₀ N ^e	2	<i>d</i>			C ₂₁ H ₂₈ N ₂ O ₂
29	Me	Me	C ₅ H ₁₁ N ₂ ^e	2	<i>d</i>			C ₂₁ H ₂₉ N ₃ O ₂
30	Me	Me	C ₄ H ₈ NO ^e	2	160–162	A	100	C ₂₀ H ₂₆ N ₂ O ₃ (C, H, N)

^aA = ethyl acetate; B = benzene; C = petroleum ether, bp 40–60°. ^bYields are based on the acids described in Table I. ^cMicroanalyses were obtained for the elements indicated in parentheses; all results were within $\pm 0.4\%$ of the calculated values. ^dObtained as an oil, homogeneous by TLC, which was used directly in the next reaction. No elemental analysis was obtained. ^eC₅H₁₀N = piperidino; C₅H₁₁N₂ = *N*-methylpiperazino; C₄H₈NO = morpholino.

In an analogous manner the amines 39–46, 51, and 54–60 were prepared. Chemical data on these compounds are collected in Table III.

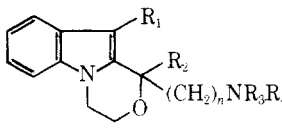
Path B. 3,4-Dihydro-10-methyl-1-propyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-ethanol (32). The acid 10 (10 g, 0.035 mol) was reduced in THF (100 ml) with LiAlH₄ (2 g, 0.05 mol) during 1 hr at 0°. A conventional work-up gave the product (7 g) as an oil. Chromatography on silica gel using EtOAc-CHCl₃ (1:1) afforded 32 as an oil (6.5 g, 62%): NMR (CDCl₃) δ 0.9 (t, 3, *J* = 7 Hz, CH₃), 1.40 (m, 2, CH₂), 2.2 (m, 4, CH₂), 2.26 (m, 3, CH₃), 3.71 (t, 2, *J* = 6 Hz, CH₂O), 4.40 (m, 4, CH₂), 7.0–7.7 (m, 4, aromatic).

3,4-Dihydro-1,10-dimethyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-butanol (33). Reduction of the acid 11 with LiAlH₄ followed by chromatography, as above, gave the product as an oil in a quantitative yield: NMR (CDCl₃) δ 1.58 (s, 3, CH₃), 2.28 (s, 3, CH₃), 3.54 (t, 2, CH₂O), 4.03 (m, 4, CH₂), 7.0–7.7 (m, 4, aromatic).

3,4-Dihydro-10-methyl-1-propyl-1,4-oxazino[4,3-*a*]indole-1-ethanol Tosylate (34). Compound 32 (1.4 g, 0.005 mol) was treated with *p*-toluenesulfonyl chloride (1.0 g, 0.006 mol) and pyridine (10 ml) at 0° for 1 hr. A conventional work-up procedure gave 2 g (91%) of the product as an oil: ir (CHCl₃) 1600, 1370, 1190, 1170 cm⁻¹.

3,4-Dihydro-1,10-dimethyl-1*H*-1,4-oxazino[4,3-*a*]indole-1-butanol Tosylate (35). The reaction of compound 33 (18.3 g, 0.067 mol) with *p*-toluenesulfonyl chloride (15 g, 0.079 mol) as above gave 26.6 g (93%) of 35 as an oil: ir (CHCl₃) 1600, 1370, 1190, 1170 cm⁻¹.

3,4-Dihydro-10-methyl-1-propyl-1-(2-iodoethyl)-1*H*-1,4-oxazino[4,3-*a*]indole (36). The tosylate 34 (2 g, 0.0047 mol) was allowed to react with NaI (6 g, 0.04 mol) in acetone at 22° for 24 hr. A conventional work-up gave an oil that was chromatographed on silica gel with C₆H₆ to afford 1 g (56%) of 36: NMR (CDCl₃) δ 0.9

Table III. Chemical and Biological Data on 1-Substituted 3,4-Dihydro-1,10-dialkyl-1*H*-1,4-oxazino[4,3-*a*]indoles


No.	R ₁	R ₂	n	NR ₃ R ₄	Mp, °C	Recrystn solvent ^a	Yield, % ^b	Formula ^{c,d}	Acute tox-icity, LD ₅₀ , mg/kg ip	Prevention of reserpine ptosis, ED ₅₀ , mg/kg ip
38	Me	Me	2	NMe ₂	237–239	A, B	33	C ₁₇ H ₂₄ N ₂ O·HCl	90	2.3
39	Me	Me	2	NHMe	249–251	C	68	C ₁₆ H ₂₂ N ₂ O·HBr	170	8.4
40	Me	Me	2	NHEt	196–198	B, C	38	C ₁₇ H ₂₄ N ₂ O·HBr	225	6.7
41	Me	Me	2	NEt ₂	191–193	B, C	33	C ₁₉ H ₂₈ N ₂ O·HBr	90	>25
42	Me	Me	3	NHEt	220–222	B, D	59	C ₁₈ H ₂₆ N ₂ O·HCl	90	15
43	Me	Me	3	NHMe	193–195	B, C	88	C ₁₇ H ₂₄ N ₂ O·HCl	125	0.5
44	Me	Me	3	NH ₂	204–206	A, B	40	C ₁₆ H ₂₂ N ₂ O·HCl	160	4.6
45	Me	Me	3	NMe ₂	200–201	A, B	47	C ₁₈ H ₂₆ N ₂ O·HCl	125	2.9
46	Me	Me	3	NEt ₂	174–176	C	60	C ₂₀ H ₃₀ N ₂ O·HBr	90	>25
47	Me	Me	4	NHMe	166–168	C	60	C ₁₈ H ₂₆ N ₂ O·HCl	90	15.3
48	Me	Me	4	NMe ₂	194–196	C	90	C ₁₉ H ₂₈ N ₂ O·HCl		>10
49	Me	Me	4	NHEt	144–146	C	70	C ₁₉ H ₂₈ N ₂ O·HCl	90	>15
50	Me	<i>n</i> -Pr	2	NHMe	229–230	C	26	C ₁₈ H ₂₆ N ₂ O·HCl	90	>10
51	Me	<i>n</i> -Pr	2	NMe ₂	196–197	C	37	C ₁₉ H ₂₈ N ₂ O·HCl	225	23
52	Me	<i>n</i> -Pr	2	NHEt	212–214	C	20	C ₁₉ H ₂₈ N ₂ O·HCl	120	>10
53	Me	<i>n</i> -Pr	2	NEt ₂	165–167	C	27	C ₂₁ H ₃₂ N ₂ O·HBr		>30
54	Et	Me	3	NHMe	157–159	B, C	84	C ₁₈ H ₂₆ N ₂ O·HCl	125	4.2
55	Me	Me	2	C ₅ H ₁₀ N ^e	253–255	A	44	C ₂₀ H ₂₈ N ₂ O·HBr	90	>25
56	Me	Me	2	C ₅ H ₁₁ N ₂ ^e	196–198	A	21	C ₂₀ H ₂₈ N ₃ O ^f 2C ₄ H ₈ O ₄ ^f	225	>35
57	Me	Me	2	C ₄ H ₈ NO ^e	234–236	B, C	80	C ₁₉ H ₂₆ N ₂ O ₂ ·HCl	225	>35
58	Me	Me	3	C ₅ H ₁₀ N ^e	205–207	C	72	C ₂₁ H ₃₀ N ₂ O·HBr	70	>20
59	Me	Me	3	C ₅ H ₁₁ N ₂ ^e	260–262	A	47	C ₂₁ H ₃₁ N ₃ O·2HBr	225	>60
60	Me	Me	3	C ₄ H ₈ NO ^e	210–212	C	46	C ₂₀ H ₂₈ N ₂ O ₂ ·HCl	190	20.5
61	Amitriptyline								94	4.7
62	Imipramine								115	6

^aA = methanol; B = ether; C = 2-propanol; D = ethanol. ^bOverall yield from the acids described in Table I. ^cAll compounds were analyzed for all elements except oxygen. All results were within $\pm 0.4\%$ of the calculated values. ^dAll compounds were prepared by LiAlH₄ reduction of the corresponding amides (path A) with the exception of 47–50 and 52 which were made by the alkylation route (path B) and 53 which was made by NaBH₄ reduction of the ethoxyiminium salt 31 (see Experimental Section). ^eC₅H₁₀N = piperidino; C₅H₁₁N₂ = *N*-methylpiperazino; C₄H₈NO = morpholino. ^fA dimaleate salt.

(t, 3, *J* = 6 Hz, CH₃), 2.31 (s, 3, CH₃), 4.06 (m, 4, CH₂), 7.21 (m, 4, aromatic).

3,4-Dihydro-1,10-dimethyl-1-(4-iodobutyl)-1*H*-1,4-oxazino[4,3-*a*]indole (37). The tosylate 34 (8.3 g, 0.02 mol) on reaction with NaI (15 g, 0.1 mol) as above gave 7.3 g (98%) of 37: mp 60–62° (petroleum ether, bp 40–60°); NMR (CDCl₃) δ 1.6 (t, 3, CH₃), 2.29 (s, 3, CH₃), 3.10 (t, 2, CH₂), 4.04 (m, 4, CH₂), 7.20 (m, 4, aromatic).

3,4-Dihydro-1,10-dimethyl-1-(4-(methylamino)butyl)-1*H*-1,4-oxazino[4,3-*a*]indole (47). Compound 37 (3.5 g, 0.0094 mol) and 100 ml of 40% aqueous methylamine in 100 ml of THF was stirred at 22° for 6 hr. Most of the THF was removed in vacuo. A conventional work-up gave 2 g (75% yield) of an oil which was converted into the HCl salt, mp 166–168° (2-PrOH).

In a similar manner compounds 48–50 and 52 were prepared. The chemical data for these compounds are collected in Table III.

3,4-Dihydro-1-[2-(diethylamino)ethyl]-10-methyl-1-propyl-1*H*-1,4-oxazino[4,3-*a*]indole (53). Triethyloxonium fluoroborate (3.5 g, 0.0185 mol) and compound 23 (5.5 g, 0.016 mol) in 100 ml of dry CH₂Cl₂ were stirred at 22° for 20 hr. The CH₂Cl₂ was removed and the residue dissolved in 50 ml of absolute EtOH. NaBH₄ (1.35 g, 0.035 mol) was added portionwise to the stirring solution at 0°. After the addition, stirring was continued at 22° for 18 hr. A conventional work-up afforded an oil that was directly converted into its HBr salt: mp 165–167° (see Table III).

Note: The ring system of the title compound should be named 1*H*-[1,4]oxazino[4,3-*a*]indole throughout.

References and Notes

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