1. Chemistry. Melting points were determined using a Reichert Köfler hot-stage apparatus and are uncorrected. Infrared spectra were recorded with a Nicolet-Avatar 360 FT-IR spectrophotometer in Nujol mulls. Routine nuclear magnetic resonance spectra were recorded in DMSO-d_6 solution on a Varian Gemini 200 spectrometer operating at 200 MHz. Evaporation was performed in vacuo (rotary evaporator). Analytical TLC was carried out on Merck 0.2 mm precoated silica gel aluminum sheets (60 F-254). Elemental analyses were performed by our Analytical Laboratory and agreed with theoretical values to within ± 0.4%.

2-Phenylindole **32** was from Sigma-Aldrich; 2-(4-fluorophenyl)indole **34** was from Lancaster. Compounds **28**,[1] **29**,[2] **30**,[3] and **31**,[4] were prepared in accordance with reported procedures.

General Procedure for the Synthesis of 5-Substituted-2-(4-substitutedphenyl)indole Derivatives 33, 35-37. A stirred solution of 50 mmol of the appropriate benzamide **28-31** (3-6) in 25 mL of dry THF, maintained under an N_2 atmosphere and at an internal temperature of –25 to 0°C, was treated dropwise with 9.3 mL (15 mmol) of n-BuLi (1.6 M solution in hexane). The stirred mixture was kept at room temperature for 24-48 h (TLC analysis), cooled in an ice bath and acidified to pH = 5-6 with diluted HCl. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2. After drying ($MgSO_4$), the combined organic phases were evaporated to dryness, furnishing the crude indoles **33**, **35-37**, which were purified by flash-chromatography (eluting system: cyclohexane-ethyl acetate in varying ratios) and/or by recrystallization from the appropriate solvent.

2-(4-Chlorophenyl)indole 33. Yield: 85%. Mp: 202-204 °C (cyclohexane) (lit. 5, mp: 208-211 °C).

2-(4-Methylphenyl)indole 35. Yield: 75%. Mp: 215-218 °C (ethyl acetate) (lit. 6, mp: 219-219.5 °C).

5-Chloro-2-phenylindole 36. Yield: 88%. Mp: 192-194 °C (toluene) (lit. 3, mp: 195-196 °C).

5-Chloro-2-(4-chlorophenyl)indole 37. Yield: 80%. Mp: 190-192 °C (lit. 4).

General Procedure for the Synthesis of [5-Substituted-2-(4-substitutedphenyl)indol-3-yl]glyoxylyl Chloride Derivatives 38-43. Oxalyl chloride (0.12 mL, 1.4 mmol) was added dropwise, at 0 °C, to a well-stirred mixture of the appropriate indole **32-37** (1.0 mmol) in 5 mL di anhydrous ethyl ether. The reaction was maintained at room temperature for 1-2 h (TLC analysis). The precipitate formed was collected and washed with portions of anhydrous ethyl ether to give the acid chlorides **38-43**, which were directly used for the next reaction.

(2-Phenylindol-3-yl)glyoxylyl chloride 38. Yield: 68%. Mp: 132-134 °C (lit. 7, mp: 132-135 °C).

[2-(4-Chlorophenyl)indol-3-yl]glyoxylyl chloride 39. Yield: 96%. Mp: 113-115 °C.

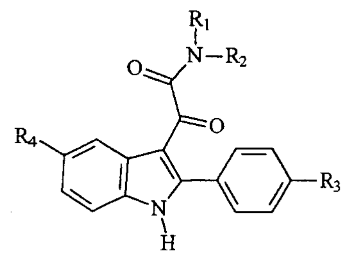
[2-(4-Fluorophenyl)indol-3-yl]glyoxylyl chloride 40. Yield: 73%. Mp: 189-190 °C (lit. 8, mp: 145 °C).

[2-(4-Methylphenyl)indol-3-yl]glyoxylyl chloride 41. Yield: 83%. Mp: 194-198 °C.

(5-Chloro-2-phenylindol-3-yl)glyoxylyl chloride 42. Yield: 67%. Mp: 116-118 °C (lit. 9, mp: 118-120 °C).

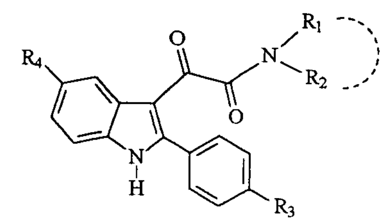
[5-Chloro-2-(4-chlorophenyl)indol-3-yl]glyoxylyl chloride 43. Yield: 65%. Mp: 125-128 °C.

TABLE 1. Physical Properties of Compounds **1-27**.



n.	R_1	R_2	R_3	R_4	yield, (%)	recryst. solvent	mp, (°C)	formula[a]
1	$(CH_2)_2CH_3$	H	H	H	55	benzene	218-220	$C_{19}H_{18}N_2O_2$
2	$(CH_2)_3CH_3$	H	H	H	55	toluene	209-210	$C_{20}H_{20}N_2O_2$
3	CH_2CH_3	CH_2CH_3	H	H	54	toluene	142-145	$C_{20}H_{20}N_2O_2$
4	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	H	H	50	petroleum benzine 60-80°C	124-126	$C_{22}H_{24}N_2O_2$
5	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	H	H	62		oil	$C_{24}H_{28}N_2O_2$
6	$(CH_2)_4CH_3$	$(CH_2)_4CH_3$	H	H	85		oil	$C_{26}H_{32}N_2O_2$
7	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	H	H	59		oil	$C_{28}H_{36}N_2O_2$
8	$CH(CH_3)_2$	$CH(CH_3)_2$	H	H	67	petroleum benzine 60-80°C	125-128	$C_{22}H_{24}N_2O_2$
9	$CH(CH_3)CH_2CH_3$	$CH(CH_3)CH_2CH_3$	H	H	55		154-156	$C_{24}H_{28}N_2O_2$
10	$-(CH_2)_4-$		H	H	71	toluene	217-221	$C_{20}H_{18}N_2O_2$

TABLE 2. Spectral Data of Compounds **1-27**.



n.	**R$_1$**	**R$_2$**	**R$_3$**	**R$_4$**	**^{1}H-NMR** (δ ppm)	**IR** (cm^{-1})
1	$(CH_2)_2CH_3$	H	H	H	0.76 (t, 3H, *J=7.4Hz*, CH_3); 1.19-1.26 (m, 2H, CH_2*CH$_2$*CH_3); 2.66-2.74 (m, 2H, *CH$_2$*CH_2CH_3); 7.23-7.27 (m, 2H, 5-H, 6-H); 7.46-7.55 (m, 6H, Ar-H); 8.05-8.10 (m, 1H, 4-H); 8.49 (t, 1H, *J=5.6Hz*, CONH, exch. with D_2O).	3350, 3100, 1645, 1590, 1420, 740.
2	$(CH_2)_3CH_3$	H	H	H	0.82 (t, 3H, *J=6.2Hz*, CH_3); 1.17-1.19 (m, 4H, CH_2(*CH$_2$*)$_2$$CH_3$); 2.72-2.75 (m, 2H, *CH$_2$*$(CH_2)_2CH_3$); 7.23-7.28 (m, 2H, 5-H, 6-H); 7.46-7.52 (m, 6H, Ar-H); 8.06-8.10 (m, 1H, 4-H); 8.43 (t, 1H, *J=5.3Hz*, CONH, exch. with D_2O); 12.38 (bs, 1H, 1-NH, exch. with D_2O).	3400, 3160, 1660, 1600, 1420, 740.
3	CH_2CH_3	CH_2CH_3	H	H	0.78 (t, 3H, *J=7.1Hz*, CH_3); 1.01 (t, 3H, *J=6.9Hz*, CH_3); 3.00 (q, 2H, *J=7.0Hz*, CH_2); 3.14 (q, 2H, *J=7.0Hz*, CH_2); 7.25-7.29 (m, 2H, 5-H, 6-H); 7.46-7.59 (m, 6H, Ar-H); 8.07-8.11 (m, 1H, 4-H); 12.42 (bs, 1H, NH, exch. with D_2O).	3175, 1610, 1580, 1420, 1075, 740.

4	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	H	H	0.65-0.78 (m, 6H, 2 CH_3); 1.17-1.24 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 1.39-1.46 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 2.90 (t, 2H, *J=7.8Hz*, $\mathit{CH_2}CH_2CH_3$); 3.03 (t, 2H, *J=7.6Hz*, $\mathit{CH_2}CH_2CH_3$); 7.24-7.28 (m, 2H, 5-H, 6-H); 7.46-7.57 (m, 6H, Ar-H); 8.03-8.07 (m, 1H, 4-H).	3170, 1610, 1580, 1420, 1075, 740.
5	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	H	H	0.69-0.87 (m, 6H, 2 CH_3); 1.04-1.40 (m, 8H, 2 $CH_2(\mathit{CH_2})_2CH_3$); 2.94-3.09 (m, 4H, 2 $\mathit{CH_2}(CH_2)_2CH_3$); 7.21-7.32 (m, 2H, 5-H, 6-H); 7.46-7.63 (m, 6H, Ar-H); 8.04-8.08 (m, 1H, 4-H); 12.43 (bs, 1H, NH, exch. with D_2O).	3200, 1620, 1590, 1420, 1100, 740.
6	$(CH_2)_4CH_3$	$(CH_2)_4CH_3$	H	H	0.71-0.86 (m, 6H, 2 CH_3); 1.24-1.45 (m, 8H, 2 $CH_2CH_2(\mathit{CH_2})_2CH_3$); 1.57-1.63 (m, 4H, 2 $CH_2\mathit{CH_2}(CH_2)_2CH_3$); 2.92-3.08 (m, 4H, 2 $\mathit{CH_2}CH_2(CH_2)_2CH_3$); 7.24-7.27 (m, 2H, 5-H, 6-H); 7.47-7.63 (m, 6H, Ar-H); 7.99-8.03 (m, 1H, 4-H); 12.40 (bs, 1H, NH, exch. with D_2O).	3200, 1610, 1580, 1420, 1100, 750.
7	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	H	H	0.82 (t, 3H, *J=6.6Hz*, CH_3); 0.90 (t, 3H, *J=6.4Hz*, CH_3); 1.06-1.27 (m, 12H, 2 $CH_2CH_2(\mathit{CH_2})_3CH_3$); 1.33-1.42 (m, 4H, 2 $CH_2\mathit{CH_2}(CH_2)_3CH_3$); 2.94-3.19 (m, 4H, 2 $\mathit{CH_2}CH_2(CH_2)_3CH_3$); 7.23-7.31 (m, 2H, 5-H, 6-H); 7.49-7.61 (m, 6H, Ar-H); 8.03-8.07 (m, 1H, 4-H); 12.44 (bs, 1H, NH, exch. with D_2O).	3200, 1615, 1580, 1420, 1100, 750.
8	$CH(CH_3)_2$	$CH(CH_3)_2$	H	H	0.98 (d, 6H, *J=6.6Hz*, $CH(\mathit{CH_3})_2$); 1.13 (d, 6H, *J=6.6Hz*, $CH(\mathit{CH_3})_2$); 3.32-3.38 (m, 1H, CH); 3.61-3.68 (m, 1H, CH); 7.24-7.29 (m, 2H, 5-H, 6-H); 7.45-7.51 (m, 4H, Ar-H); 7.62-7.65 (m, 2H, Ar-H); 8.09-8.13 (m, 1H, 4-H); 12.42 (bs, 1H, NH, exch. with D_2O).	3200, 1620, 1590, 1420, 1140, 750.

9	$CH(CH_3)CH_2CH_3$	$CH(CH_3)CH_2CH_3$	H	H	0.64 (t, 3H, *J=7.3Hz*, CH_2CH_3); 0.78 (t, 3H, *J=7.5Hz*, CH_2CH_3); 1.07 (d, 3H, *J=6.6Hz*, $CHCH_3$); 1.14 (d, 3H, *J=6.6Hz*, $CHCH_3$); 1.43-1.60 (m, 2H, CH_2); 1.71-1.89 (m, 2H, CH_2); 2.94-3.05 (m, 2H, 2 CH); 7.23-7.28 (m, 2H, 5-H, 6-H); 7.45-7.52 (m, 4H, Ar-H); 7.63-7.68 (m, 2H, Ar-H); 8.06-8.11 (m, 1H, 4-H); 12.42 (bs, 1H, NH, exch. with D_2O).	3150, 1610, 1580, 1420, 1190, 750.
10	$-(CH_2)_4-$		H	H	1.54-1.72 (m, 4H, $CH_2(CH_2)_2CH_2$); 2.79 (t, 2H, *J=6.4Hz*, CH_2N); 3.21 (t, 2H, *J=6.8Hz*, CH_2N); 7.22-7.36 (m, 2H, 5-H, 6-H); 7.46-7.51 (m, 6H, Ar-H); 8.14-8.18 (m, 1H, 4-H); 12.45 (bs, 1H, NH, exch. with D_2O).	3200, 1630, 1590, 1410, 1180, 750.
11	$-(CH_2)_5-$		H	H	1.18-1.46 (m, 6H, $CH_2(CH_2)_3CH_2$); 3.01-3.11 (m, 4H, CH_2NCH_2); 7.23-7.30 (m, 2H, 5-H, 6-H); 7.41-7.59 (m, 6H, Ar-H); 8.12-8.16 (m, 1H, 4-H); 12.48 (bs, 1H, NH, exch. with D_2O).	3200, 1620, 1590, 1420, 1100, 750.
12	$-(CH_2)_6-$		H	H	1.28-1.51 (m, 8H, $CH_2(CH_2)_4CH_2$); 2.94 (t, 2H, *J=5.4Hz*, CH_2N); 3.19 (t, 2H, *J=5.5Hz*, CH_2N); 7.25-7.29 (m, 2H, 5-H, 6-H); 7.46-7.58 (m, 6H, Ar-H); 8.11-8.16 (m, 1H, 4-H); 12.46 (bs, 1H, NH, exch. with D_2O).	3190, 1620, 1590, 1420, 1100, 750.
13	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	Cl	H	0.63-0.81 (m, 6H, 2 CH_3); 1.15-1.29 (m, 2H, $CH_2CH_2CH_3$); 1.39-1.50 (m, 2H, $CH_2CH_2CH_3$); 2.92-3.07 (m, 4H, 2 $CH_2CH_2CH_3$); 7.24-7.27 (m, 2H, 5-H, 6-H); 7.47-7.60 (m, 5H, Ar-H); 8.02-8.05 (m, 1H, 4-H); 12.50 (bs, 1H, NH, exch. with D_2O).	3200, 1615, 1580, 1420, 1090, 750.
14	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	Cl	H	0.73 (t, 3H, *J=7.2Hz*, CH_3); 0.87 (t, 3H, *J=6.3Hz*, CH_3); 1.00-1.49 (m, 8H, 2 $CH_2(CH_2)_2CH_3$); 2.96-3.08 (m, 4H, 2 $CH_2(CH_2)_2CH_3$); 7.22-7.33 (m, 2H, 5-H, 6-H); 7.45-7.64 (m, 5H, Ar-H); 8.04-8.08 (m, 1H, 4-H); 12.47 (bs, 1H, NH, exch. with D_2O).	3220, 1610, 1570, 1440, 1100, 750.

15	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	Cl	H	0.74 (t, 3H, *J=6.5Hz*, CH_3); 0.87 (t, 3H, *J=6.4Hz*, CH_3); 1.07-1.40 (m, 16H, 2 $CH_2(\mathit{CH_2})_4CH_3$); 3.00-3.07 (m, 4H, 2 $\mathit{CH_2}(CH_2)_4CH_3$); 7.24-7.30 (m, 2H, 5-H, 6-H); 7.47-7.64 (m, 5H, Ar-H); 8.04-8.07 (m, 1H, 4-H); 12.50 (bs, 1H, NH, exch. with D_2O).	3230, 1615, 1570, 1420, 1100, 740.
16	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	F	H	0.65-0.80 (m, 6H, 2 CH_3); 1.18-1.30 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 1.39-1.51 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 2.91-3.07 (m, 4H, 2 $\mathit{CH_2}CH_2CH_3$); 7.20-7.70 (m, 7H, Ar-H); 8.01-8.06 (m, 1H, 4-H); 12.50 (bs, 1H, NH, exch. with D_2O).	3250, 1610, 1590, 1420, 1100, 760.
17	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	F	H	0.72 (t, 3H, *J=7.3Hz*, CH_3); 0.85 (t, 3H, *J=6.3Hz*, CH_3); 1.04-1.48 (m, 8H, 2 $CH_2(\mathit{CH_2})_2CH_3$); 2.98-3.10 (m, 4H, 2 $\mathit{CH_2}(CH_2)_2CH_3$); 7.23-7.67 (m, 7H, Ar-H); 8.05-8.09 (m, 1H, 4-H); 12.40 (bs, 1H, NH, exch. with D_2O).	3180, 1610, 1590, 1420, 1200, 750.
18	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	F	H	0.74 (t, 3H, *J= 6.5Hz*, CH_3); 0.87 (t, 3H, *J=6.6Hz*, CH_3); 1.06-1.50 (m, 16H, 2 $CH_2(\mathit{CH_2})_4CH_3$); 2.88-3.07 (m, 4H, 2 $\mathit{CH_2}(CH_2)_4CH_3$); 7.20-7.68 (m, 7H, Ar-H); 8.03-8.07 (m, 1H, 4-H); 12.45 (bs, 1H, NH, exch. with D_2O).	3210, 1620, 1590, 1420, 1100, 670.
19	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	CH_3	H	0.65-0.80 (m, 6H, 2 CH_3); 1.13-1.24 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 1.38-1.49 (m, 2H, $CH_2\mathit{CH_2}CH_3$); 2.39 (s, 3H, 4'-CH_3); 2.90-3.05 (m, 4H, 2 $\mathit{CH_2}CH_2CH_3$); 7.13-7.32 (m, 4H, Ar-H); 7.44-7.49 (m, 3H, Ar-H); 8.01-8.05 (m, 1H, 4-H); 12.39 (bs, 1H, NH, exch. with D_2O).	3180, 1600, 1590, 1420, 1090, 740.

20	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	CH_3	H	0.72 (t, 3H, *J=7.2Hz*, CH_3); 0.84 (t, 3H, *J=6.4Hz*, CH_3); 1.03-1.44 (m, 8H, 2 $CH_2(CH_2)_2CH_3$); 2.39 (s, 3H, 4'-CH_3); 2.94-3.07 (m, 4H, 2 $CH_2(CH_2)_2CH_3$); 7.22-7.32 (m, 4H, Ar-H); 7.44-7.49 (m, 3H, Ar-H); 8.03-8.07 (m, 1H, 4-H); 12.37 (bs, 1H, NH, exch. with D_2O).	3200, 1610, 1590, 1420, 1100, 750.
21	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	CH_3	H	0.74 (t, 3H, *J=6.6Hz*, CH_3); 0.87 (t, 3H, *J=6.6Hz*, CH_3); 1.06-1.39 (m, 16H, 2 $CH_2(CH_2)_4CH_3$); 2.38 (s, 3H, 4'-CH_3); 2.90-3.10 (m, 4H, 2 $CH_2(CH_2)_4CH_3$); 7.22-7.32 (m, 4H, Ar-H); 7.45-7.49 (m, 3H, Ar-H); 8.05-8.09 (m, 1H, 4-H); 12.39 (bs, 1H, NH, exch. with D_2O).	3220, 1610, 1580, 1420, 1100, 750.
22	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	H	Cl	0.66-0.78 (m, 6H, 2 CH_3); 1.13-1.31 (m, 2H, $CH_2CH_2CH_3$); 1.34-1.51 (m, 2H, $CH_2CH_2CH_3$); 2.90 (t, 2H, *J=7.7Hz*, $CH_2CH_2CH_3$); 3.03 (t, 2H, *J=7.8Hz*, $CH_2CH_2CH_3$); 7.31 (dd, 1H, *J=8.6,2.2Hz*, 6-H); 7.48-7.70 (m, 6H, Ar-H); 8.05 (d, 1H, *J=2.0Hz*, 4-H).	3170, 1610, 1580, 1420, 1100, 700.
23	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	H	Cl	0.70-0.91 (m, 6H, 2 CH_3); 1.04-1.44 (m, 8H, 2 $CH_2(CH_2)_2CH_3$); 2.95-3.08 (m, 4H, 2 $CH_2(CH_2)_2CH_3$); 7.31 (dd, 1H, *J=8.6,2.1Hz*, 6-H); 7.48-7.61 (m, 6H, Ar-H); 8.05 (d, 1H, *J=2.0Hz*, 4-H); 12.65 (bs, 1H, NH, exch. with D_2O).	3180, 1620, 1590, 1380, 1100, 760.
24	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	H	Cl	0.74 (t, 3H, *J=6.2*Hz, CH_3); 0.86 (t, 3H, *J=6.1Hz*, CH_3); 1.07-1.42 (m, 16H, 2 $CH_2(CH_2)_4CH_3$); 2.96-3.08 (m, 4H, 2 $CH_2(CH_2)_4CH_3$); 7.31 (dd, 1H, *J=9.0,1.8Hz*, 6-H); 7.48-7.60 (m, 6H, Ar-H); 8.02 (d, 1H, *J=1.6Hz*, 4-H); 12.72 (bs, 1H, NH, exch. with D_2O).	3200, 1610, 1580, 1420, 1100, 740.

25	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	Cl	Cl	0.66-0.81 (m, 6H, 2 CH_3); 1.13-1.29 (m, 2H, $CH_2CH_2CH_3$); 1.39-1.52 (m, 2H, $CH_2CH_2CH_3$); 2.92-3.07 (m, 4H, 2 $CH_2CH_2CH_3$); 7.33 (dd, 1H, *J*=8.5,2.1*Hz*, 6-H); 7.51 (d, 1H, *J*=8.6*Hz*, 7-H); 7.60-7.62 (m, 4H, ArH); 8.03 (d, 1H, *J*=1.6*Hz*, 4-H); 12.74 (bs, 1H, NH, exch. with D_2O).	3200, 1620, 1580, 1420, 1100, 720.
26	$(CH_2)_3CH_3$	$(CH_2)_3CH_3$	Cl	Cl	0.74 (t, 3H, *J*=7.2*Hz*, CH_3); 0.87 (t, 3H, *J*=6.3Hz, CH_3); 1.05-1.50 (m, 8H, 2 $CH_2(CH_2)_2CH_3$); 2.90-3.08 (m, 4H, 2 $CH_2(CH_2)_2CH_3$); 7.33 (dd, 1H, *J*=8.7,2.1*Hz*, 6-H); 7.51 (d, 1H, *J*=8.6*Hz*, 7-H); 7.59-7.62 (m, 4H, Ar-H); 8.05 (d, 1H, *J*=2.2*Hz*, 4-H); 12.72 (bs, 1H, NH, exch. with D_2O).	3230, 1610, 1580, 1420, 1100, 730.
27	$(CH_2)_5CH_3$	$(CH_2)_5CH_3$	Cl	Cl	0.75 (t, 3H, *J*=6.6*Hz*, CH_3); 0.87 (t, 3H, *J*=6.5*Hz*, CH_3); 1.07-1.41 (m, 16H, 2 $CH_2(CH_2)_4CH_3$); 2.99-3.07 (m, 4H, 2 $CH_2(CH_2)_4CH_3$); 7.32 (dd, 1H, *J*=8.5,1.9*Hz*, 6-H); 7.51 (d, 1H, *J*=8.6*Hz*, 7-H); 7.55-7.65 (m, 4H, Ar-H); 8.03 (d, 1H, *J*=1.8*Hz*, 4-H); 12.74 (bs, 1H, NH, exch. with D_2O).	3210, 1630, 1600, 1420, 1100, 730.

2. Biological Methods

Materials. [^{3}H]PK 11195 (A.S. 85.5 Ci/mmol) and [^{3}H]flumazenil (A.S. 78.6 Ci/mmol) were purchased from Perkin-Elmer Life Sciences. Culture medium, Fetal Bovine Serum (FBS), L-glutamine and antibiotics were purchased from Cambrex Bio Science. PK 11195 and Ro5-4864 were obtained from Sigma-Aldrich. 1,2,3,4-tetrahydro-4-oxo-7-chloro-2-naphthylpyridine (SU10603) and 2α,4α,5α,17β-4,5epoxy-17-hydroxy-3-oxoandrostane-2-carbonitrile (trilostane) were gifts from Novartis Farma S.p.a. and Dr D. Zister, University of Dublin, respectively. All other reagents were obtained from commercial suppliers.

[^{3}H]PK 11195 binding to rat kidney mitochondrial membranes

For binding studies, crude mitochondrial membranes were incubated with 0.6 nM [^{3}H]PK 11195 in the presence of a range of concentrations of the tested compounds (0.1 nM-10 μM) in a total volume of 0.5 mL of Tris-HCl, pH 7.4, as previously described.[10] Drugs were dissolved in DMSO, and the level of this solvent did not exceed 0.5% and was maintained constant in all tubes. For the active compounds, the IC_{50} values were determined and K_i values were derived in accordance with the equation of Cheng and Prusoff.[11]

[^{3}H]Flumazenil binding to rat cerebral cortex membranes

Rat cerebral cortex membranes, subjected to washing procedures to remove endogenous GABA, were incubated with 0.2 nM [^{3}H]flumazenil in the presence of the test compounds for 90 min at 0°C in 0.5 mL of 50 mM Tris-citrate buffer, pH 7.4, as previously described.[12]

Cell Culture

Rat C6 glioma cells were cultured in Dulbecco's Modified Eagles Medium supplemented with 10 % FBS, 2 mM L-glutamine, 100 units/mL penicillin, and 100 μg/mL streptomycin. Cultures were maintained in a humidified atmosphere of 5% CO_2/95% air at 37 °C.

Steroid Biosynthesis

The measurement of pregnenolone production of C6 cells exposed to the novel compounds or PK 11195, Ro5-4864, or clonazepam (40 μM) was performed by radioimmunoassay (RIA), as previously described.[10]

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