The Synthesis of a Series of (α-Amino)indol-3-yl Ketones

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A series of [(α-amino)indol-3-yl]-2-methyl-1-propanones and [(α-amino)indol-3-yl]cyclopentylmethanones has been synthesized by a variety of reductive reactions performed on the corresponding series of (α-azido)-indol-3-yl ketones. One of the more interesting reductive procedures involved the palladium-catalyzed decomposition of formic acid with the formation of hydrogen *in situ*. The (α-azido)ketones were prepared in excellent yield by the displacement of the tertiary bromine atom from the (α-bromo)ketones using sodium azide in *N,N*-dimethylformamide. Bromination was accomplished by using either cupric bromide in ethyl acetate/chloroform or phenyltrimethylammonium tribromide in tetrahydrofuran.

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During our synthetic efforts to produce compounds possessing psychotropic activity, a series of (α-amino)indol-3-yl ketones was investigated. They were of potential interest since they incorporate not only the 3-acyl functionality shown to impart anticonvulsant activity [1] but also the 3-aminoethyl side chain characteristic of the psychoactive tryptamines [2]. The starting indol-3-yl and 1-alkylindol-3-yl ketones (Table I) were prepared according to the routes shown in Scheme I [3].

Initial attempts to brominate **1** and **2** (Table I) using *N*-bromosuccinimide in carbon tetrachloride produced mixtures containing bromine substituted in the aromatic portion of the molecule. This is a common side reaction of indoles and is usually circumvented by acylating the indole Grignard reagent with an α-haloacyl halide [4]. The scope of this reaction limits the type of derivatives which can be prepared and was unsuitable for our purposes. Therefore, we explored other methods of bromination to produce the desired series of indole-α-bromoketones. The reaction of 3-acetylindole with bromine in cold methanol has been reported to produce the α-bromo compound in good yield [5]. However, when these reaction conditions were employed with our compounds, the desired products could not be isolated. The bromination of **1** using cupric bromide in ethyl acetate/chloroform (Method C) [6] proceeded slowly. The reaction produced a mixture of product **7** contaminated with starting material which could be easily separated by recrystallization. The starting material

Scheme I

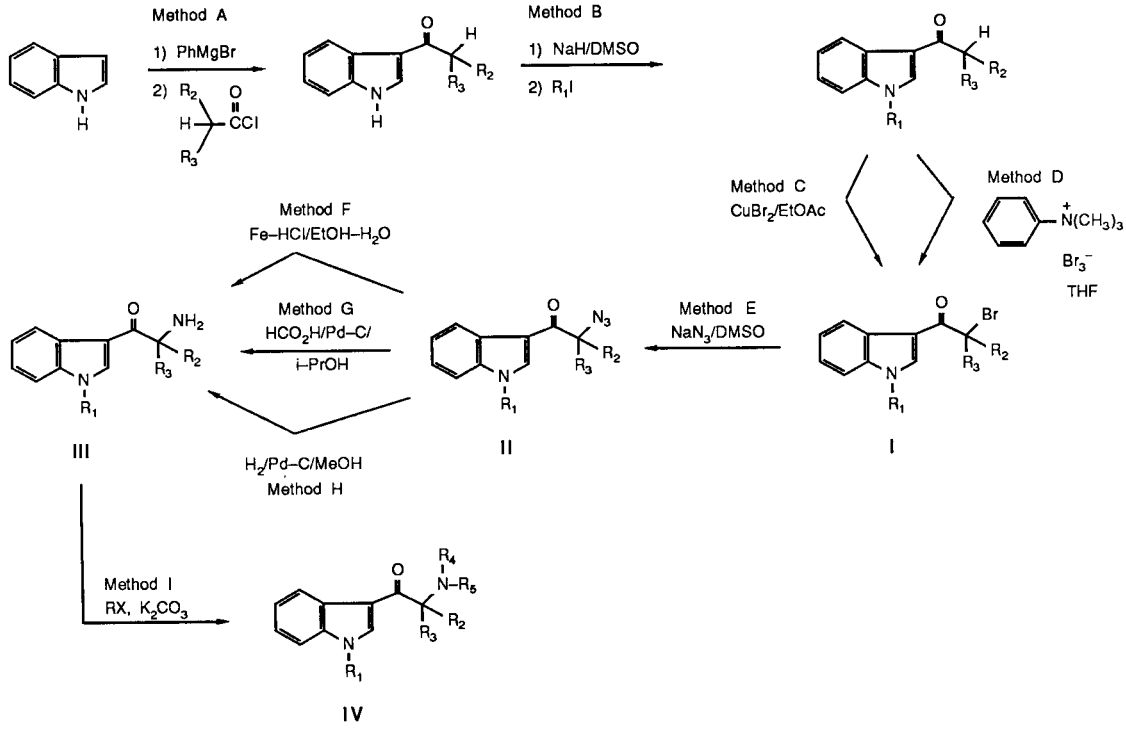
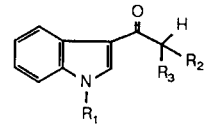


Table I

Indol-3-yl Ketones

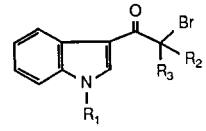


No.	R_1	R_2	R_3	mp, °C	Yield %	Crystallization Solvent [a]	Method	Formula	Analysis (%) Calcd. (Found) C	H	N
1	H	CH_3	CH_3	125-127°	50%	B-P	A	$C_{12}H_{13}NO$	76.98 (76.79)	7.00 (6.83)	7.48 (7.39)
2	CH_3	CH_3	CH_3	75-77°	89%	B-P	B	$C_{13}H_{15}NO$	77.58 (77.63)	7.51 (7.67)	4.97 (4.83)
3	CH_2CH_3	CH_3	CH_3	80-82°	87%	T-P	B	$C_{14}H_{17}NO$	78.10 (77.89)	7.96 (7.91)	6.51 (6.62)
4	$CH_2CH=CH_2$	CH_3	CH_3	59-60°	89%	C	B	$C_{15}H_{17}NO$	79.26 (79.40)	7.54 (7.60)	6.16 (6.25)
5	H	$-(CH_2)_4-$		165-167°	49%	T	B	$C_{14}H_{15}NO$	78.84 (78.54)	7.09 (6.99)	6.57 (6.47)
6	CH_3	$-(CH_2)_4-$		78-79°	86%	C-P	B	$C_{15}H_{17}NO$	79.26 (79.14)	7.54 (7.29)	6.16 (6.08)

[a] Crystallization solvents for Tables I through IV: B = benzene, C = cyclohexane, P = petroleum ether, X = xylene, E = ether, M = methanol, T = tolulene, O = 2-propanol.

Table II

(α-Bromo)indol-3-yl Ketones



No.	R_1	R_2	R_3	mp, °C	Yield %	Crystallization Solvent [a]	Method	Formula	Analysis (%) Calcd. (Found) C	H	N
7	H	CH_3	CH_3	176-178°	90-94%	X	D	$C_{12}H_{12}BrNO$	54.15 (53.96)	4.55 (4.38)	5.26 (5.14)
8	CH_3	CH_3	CH_3	107-109°	90-92%	B-P	C or D	$C_{13}H_{14}BrNO$	55.73 (55.68)	5.04 (5.13)	5.00 (5.01)
9	CH_2CH_3	CH_3	CH_3	90-92°	76%	C-P	C	$C_{14}H_{16}BrNO$	57.15 (57.23)	5.48 (5.37)	4.76 (4.71)
10	H	$-(CH_2)_4-$		162-163°	97%	X	D	$C_{14}H_{14}BrNO$	57.55 (57.61)	4.83 (4.91)	4.80 (4.95)
11	CH_3	$-(CH_2)_4-$		116-117°	90%	C-P	D	$C_{15}H_{16}BrNO$	58.83 (58.99)	5.27 (5.25)	4.58 (4.50)

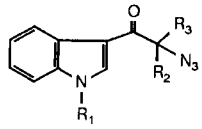
appeared to form a complex with the copper salt and could not be detected by thin layer chromatography during the course of the reaction.

A more efficient method was the use of phenyltrimethylammonium tribromide in tetrahydrofuran [7]. These complimentary methods produced the series of (α-bromo)indol-3-yl ketones (Table II).

Attempted direct displacement of the bromine atom by various primary and secondary amines (for example benzylamine, methylamine, diethylamine and pyrrolidine) which had been reported to be successful for other indol-3-yl-α-haloketones [4a,4b,5a] failed to give the desired products. Other attempts to produce useful intermediates which could be converted to amine functions were equally

Table III

(α-Azido)indol-3-yl Ketones

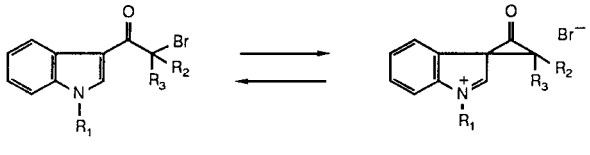


No.	R_1	R_2	R_3	mp, °C	Yield %	Crystallization Solvent [a]	Method	Formula	Analysis (%) Calcd. (Found) C	H	N
12	H	CH_3	CH_3	104-106°	93%	E-P	E	$C_{12}H_{12}N4O$	63.14 (63.35)	5.30 (5.41)	24.55 (24.74)
13	CH_3	CH_3	CH_3	59-61°	97%	E-P	E	$C_{13}H_{14}N_4O$	64.45 (64.49)	5.82 (5.78)	23.13 (23.28)
14	CH_2CH_3	CH_3	CH_3	48-49°	90%	P	E	$C_{14}H_{16}N_4O$	65.60 (65.90)	6.29 (6.36)	21.86 (21.79)
15	H	-$(CH_2)_4$-		115-116°	71%	T-P	E	$C_{14}H_{14}N_4O$	66.12 (66.55)	5.55 (5.54)	22.04 (22.19)
16	CH_3	-$(CH_2)_4$-		67-69°	86%	C-P	E	$C_{15}H_{16}N_4O$	67.14 (67.20)	6.01 (6.04)	20.88 (21.10)

unsuccessful.

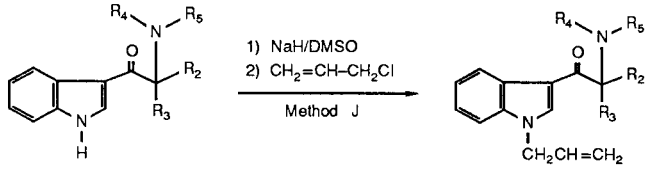
However, the nucleophilic displacement of the bromine by azide ion, which has been reported for an indol-3-yl primary bromoketone [5], proved to be an excellent general reaction to produce the corresponding series of (α-azido)-indol-3-yl ketones (Table III). The reactions proceeded rapidly and in high yield. Since the displacement center is tertiary in this case, a mechanistic consideration would necessitate the formation of an intermediate with a high degree of ionic character, perhaps one similar to that proposed in Figure 1 [8].

Figure 1



The reduction of the azide functionality under a variety of conditions [9] led to the formation of the primary (α-amino)indol-3-yl ketones (Table IV) [10]. Of particular interest is the palladium-catalyzed decomposition of formic acid with the formation of hydrogen *in situ*. This seldom used procedure provides an alternative method for some hydrogenations and has been previously used to reduce aromatic nitro compounds [11]. The resulting primary α-amino ketones could then be alkylated by employing an alkyl halide and powdered potassium carbonate in refluxing acetone (Method I) to produce the series of *N*-substituted α-amino ketones (Table IV).

Scheme II



The only deviation from these general procedures occurred in the bromination where R_1 was allyl. Evolution of gaseous hydrogen bromide during the reaction produced some addition of the hydrohalogen to the double bond and the mixture could not be satisfactorily purified. An alternative sequence of reactions where the allyl group was put on in a final alkylation step using sodium hydride and 2-propenyl chloride in dimethylsulfoxide (Scheme II) completed the desired series with the preparation of **20**, **29** and **30** (Table IV).

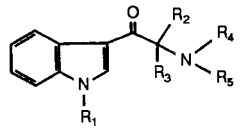
EXPERIMENTAL

Melting points were taken on a Hoover capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were determined on a Digilab FTS-14 or Nicolet FT IR SX-20 with 2 cm^{-1} resolution. Proton magnetic resonance (nmr) spectra were recorded on a Varian EM-390 or an IBM 100 WP100SY spectrometer. Chemical shifts are reported in δ units relative to internal tetramethylsilane. Mass spectra were recorded on either a Finnigan 4500 GCMS or a VG Analytical 7070E/HF with an 11/250 Data System. Solutions were dried over magnesium sulfate and concentrated on a rotary evaporator at 30-45° and pressures of 10-20 mm. All moisture sensitive reactions were carried out under a dry nitrogen atomosphere. Elemental analyses were performed on a Perkin-Elmer 240 elemental analyzer.

3-Acyl-1*H*-indoles (Table I), Method A (1,5).

Table IV

(α-Amino)indol-3-yl Ketones



No.	R_1	R_2	R_3	R_4	R_5	mp, °C	Yield	Crystallization Solvent [a]	Method	Formula	Analysis (%) Calcd. (Found) C	H	N
17	H	CH_3	CH_3	H	H	172-174°	91%	O-E	FGH	$C_{12}H_{14}N_2O$	71.26 (71.16)	6.98 (6.81)	13.85 (13.87)
18	CH_3	CH_3	CH_3	H	H	332-333°	89%	O-M-E	H	$C_{13}H_{16}N_2O\cdot HCl$	61.78 (61.57)	6.78 (6.70)	11.09 (10.98)
19	CH_2CH_3	CH_3	CH_3	H	H	333-336°	89%	O-M-E	H	$C_{14}H_{18}N_2O\cdot HCl$	63.03 (62.80)	7.18 (7.18)	10.50 (10.46)
20	$-CH_2CH=CH_2$	CH_3	CH_3	H	H	283-284°	79%	O	J	$C_{15}H_{18}N_2O\cdot HCl$	64.60 (64.59)	6.87 (6.72)	10.05 (9.98)
21	H	$-(CH_2)_4-$		H	H	146-147°	68%	O	H	$C_{14}H_{16}N_2O$	73.65 (73.73)	7.07 (6.96)	12.27 (12.31)
22	CH_3	$-(CH_2)_4-$		H	H	90-91°	85%	C	H	$C_{15}H_{18}N_2O$			
	--	--		--	--	273-275°	--	O-M-E		$C_{15}H_{18}N_2O\cdot HCl$	64.62 (64.74)	6.87 (6.96)	10.05 (9.98)
23	H	CH_3	CH_3	CH_3	CH_3	138-139°	76%	C-P	I	$C_{14}H_{18}N_2O$	73.01 (73.19)	7.87 (7.82)	12.17 (12.17)
24	H	CH_3	CH_3	H	CH_2CH_3	134-139°	76%	CT-P	I	$C_{14}H_{18}N_2O$	73.01 (73.21)	7.87 (7.80)	12.17 (12.26)
25	CH_3	CH_3	CH_3	CH_3	CH_3	142-143°	67%	C-P	I	$C_{15}H_{20}N_2O$	73.73 (73.58)	8.25 (8.39)	11.47 (11.27)
26	CH_3	CH_3	CH_3	H	CH_2CH_3	328-329°	90%	M-E	I	$C_{15}H_{20}N_2O\cdot HCl$	64.15 (63.98)	7.54 (7.57)	9.98 (9.89)
27	CH_2CH_3	CH_3	CH_3	CH_3	CH_3	260-262°	63%	OM-E	I	$C_{16}H_{22}N_2O\cdot HCl$	65.18 (65.46)	7.86 (7.80)	9.50 (9.63)
28	CH_2CH_3	CH_3	CH_3	H	CH_2CH_3	290-292°	67%	O-E	I	$C_{16}H_{22}N_2O\cdot HCl$	65.18 (64.98)	7.86 (7.91)	9.50 (9.33)
29	$-CH_2-CH=CH_2$	CH_3	CH_3	CH_3	CH_3	258-260°	91%	O-M	J	$C_{17}H_{22}N_2O\cdot HCl$	66.54 (66.67)	7.56 (7.42)	9.13 (9.07)
30	$-CH_2-CH=CH_2$	CH_3	CH_3	H	CH_2CH_3	270-272°	78%	O-M	J	$C_{17}H_{22}N_2O\cdot HCl$	66.54 (66.77)	7.56 (7.41)	9.13 (9.18)
31	H	$-(CH_2)_4-$		H	CH_2CH_3	224-225°	40%	O-E	I	$C_{16}H_{20}N_2O\cdot HCl$	65.63 (65.82)	7.23 (7.24)	9.57 (9.63)
32	CH_3	$-(CH_2)_4-$		CH_3	CH_3	119-120°	71%	O	I	$C_{17}H_{22}N_2O$	75.52 (75.79)	8.20 (8.35)	10.36 (10.47)
33	CH_3	$-(CH_2)_4-$		H	CH_2CH_3	277-279°	71%	M	I	$C_{17}H_{22}N_2O\cdot HCl$	66.54 (66.84)	7.56 (7.43)	9.13 (9.04)

(1*H*-Indol-3-yl)cyclopentylmethanone (**5**).

To a solution of 2.8 moles of phenylmagnesium bromide in 2 l of anhydrous ether [prepared from 440 g (2.8 moles) of bromobenzene and 68.0 g (2.8 g-atoms) of magnesium turnings] was added dropwise a solution of 328 g (2.8 moles) of 1*H*-indole in 800 ml of benzene. The resulting solution was stirred for ten minutes and treated dropwise with a solution of 322 g (2.4 moles) of cyclopentane carbonyl chloride in 800 ml of benzene. The reaction was stirred at reflux for one hour and decomposed by the careful addition of 1 l of water. The organic precipitate was removed by filtration and dried *in vacuo* to give 169 g of crude **5**, mp 159-163°. The filtrate was separated into an aqueous and organic layer and the organic layer was dried and concentrated to give an additional 97 g of **5**, mp 161-165°. The two fractions were combined and recrystallized from toluene to give 250 g (49%) of crystalline **5**, mp 165-167°; IR (KBr): 3178, 2842, 1618 cm^{-1}; nmr (DMSO-d_6): δ 1.48-2.06 (m, 8H), 3.52 (m, 1H), 7.08-7.63 (m, 3H), 8.15-8.39 (m, 1H), 8.33 (s, 1H).

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.54; H, 6.99; N, 6.48.

1-Alkyl-3-indolyl Ketones (Table I), Method B (**2**, **3**, **4**, **6**).

2-Methyl-1-(1-methyl-1*H*-indol-3-yl)-1-propanone (**2**).

To a suspension of 46.0 g (1.04 moles) of 54.3% sodium hydride/mineral oil in 250 ml of dry dimethylsulfoxide at 20° was added dropwise a solution of 187 g (1.0 mole) of **1** in 250 ml of dimethylsulfoxide, keeping the temperature below 25°. When the addition was complete, the reaction was heated to 40° until hydrogen evolution ceased. After cooling to

25°, 156.0 g (1.1 moles) of methyl iodide was added dropwise, keeping the temperature below 30°. The mixture was stirred for 15 minutes after the addition was complete and poured onto 4 l of ice and water. The resulting crystalline solid was removed by filtration, dissolved in toluene, washed copiously with water and dried. After concentrating, the residue was diluted with petroleum ether to give 179 g (89%) of crystalline **2**, mp 75-76° [8].

3-(α-Bromo)acylindoles Table II, Method C (**8**, **9**).

2-Bromo-1-(1-ethyl-1*H*-indol-3-yl)-2-methyl-1-propanone (**9**).

To a refluxing suspension of 362 g (1.62 moles) of cupric bromide in 1.2 l of ethyl acetate was added rapidly a solution of 166 g (0.77 mole) of **3** in 250 ml of chloroform. The mixture was stirred at reflux for 18 hours, cooled to 20° and filtered through Celite. The filtrate was diluted with 1 l of ether, washed with water, dried, treated with charcoal, filtered through Celite and the filtrate concentrated. The residue was triturated with petroleum ether to give 171 g (76%) of crystalline **9**, mp 88-90°. Recrystallization of a sample from cyclohexane/petroleum ether gave, mp 90-92°; ir (potassium bromide): 1628, 1518 cm^{-1}; nmr (deuteriochloroform): δ 1.52 (t, 3H), 2.08 (s, 6H), 4.24 (q, 2H), 7.08-7.42 (m, 3H), 8.47 (s, 1H), 8.33 (m, 1H).

Anal. Calcd. for $C_{14}H_{16}BrNO$: C, 57.15; H, 5.48; N, 4.76; Br, 27.07. Found: C, 57.23; H, 5.37; N, 4.71; Br, 26.85.

3-(α-Bromo)acylindoles (Table II), Method D (**7**, **8**, **10**, **11**).

(1-Bromocyclopentyl)(1*H*-indol-3-yl)methanone (**10**).

To a solution of 188 g (0.5 mole) of phenyltrimethylammonium tribromide in 1 l of tetrahydrofuran was added 107 g (0.5 mole) of **5** all at once. The reaction was stirred at 35° for 18 hours and the precipitated phenyltrimethylammonium bromide was removed by filtration. The filtrate was concentrated and the residue triturated with petroleum ether to give 141 g (97%) of **10** as a crystalline solid, mp 160-161°. Recrystallization of a sample from xylene gave, mp 162-163°; ir (potassium bromide): 1643, 1530 cm^{-1}; nmr (deuteriochloroform): δ 1.58-2.17 (m, 4H), 2.28-2.67 (m, 4H), 7.18-7.67 (m, 3H), 8.19-8.38 (m, 2H), 12.1 (bs, 1H).

Anal. Calcd. for $C_{14}H_{14}BrNO$: C, 57.55; H, 4.83; N, 4.80. Found: C, 57.61; H, 4.91; N, 4.94.

3-(α-Azido)acylindoles (Table III), Method E (**12-16**).

2-Azido-2-methyl-1-(1-methyl-1*H*-indol-3-yl)-1-propanone (**13**).

To a suspension of 48 g (0.75 mole) of sodium azide in 500 ml dimethylsulfoxide was added portionwise 140 g (0.5 mole) of **8**, keeping the temperature below 50°. When the addition was complete, the reaction was heated at 50° for two hours, cooled to 20° and diluted with 3.5 l of ice and water. The mixture was extracted with ether (3 x 500 ml), and the combined ether layers were washed with water (4 x 500 ml), dried, treated with charcoal, and filtered through Celite. The filtrate was concentrated and the residue was crystallized by the addition of petroleum ether to give 117 g (97%) of **13**, mp 57-60°. Recrystallization from ether/petroleum ether gave, mp 59-61°; ir (potassium bromide): 3130, 3000, 2950, 2117, 1608 cm^{-1}; nmr (deuteriochloroform): δ 2.08 (s, 6H), 3.81 (s, 3H), 7.22-7.40 (m, 3H), 8.34 (s, 1H), 8.50 (m, 1H).

Anal. Calcd. for $C_{13}H_{14}N_4O$: C, 64.45; H, 5.82; N, 23.13. Found: C, 64.49; H, 5.78; N, 23.28.

3-(α-Amino)acylindoles (Table IV), Method F (**17**).

2-Amino-1-(1*H*-idol-3-yl)-2-methyl-1-propanone (**17**).

To a refluxing suspension of 12.0 g (0.22 g-atom) of reduced iron powder in a solution of 25 ml of water and 100 ml of ethanol was added 22.8 g (0.1 mole) of **12** followed by 0.5 ml of concentrated hydrochloric acid. The reaction mixture was heated at reflux for 18 hours, cooled to 20°, filtered through Celite and the filtrate concentrated. The residue was partitioned between ether and water. The water layer was separated, made basic with 50% sodium hydroxide and extracted with ether (3 x 200 ml). The combined ether layers were washed with water, dried and evaporated to give 20 g (86%) of **17**, mp 169-171°. Recrystallization of a sample from 2-propanol/ether gave pure **17**, mp 172-174°; ir (potassium bromide): 3336, 3296, 1617 cm^{-1}; nmr (DMSO -d_6): δ 1.48 (s, 6H), 7.18-7.63 (m, 3H), 8.28-8.45 (m, 1H), 8.78 (s, 1H).

Anal. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.16; H, 6.81; N, 13.87.

3-(α-Amino)acylindoles (Table IV), Method G (**17**).

2-Amino-1-(1*H*-indol-3-yl)-2-methyl-1-propanone (**17**).

To a slurry of 2.0 g of 5% palladium on carbon in 15 ml of water was added a solution of 22.8 g (0.1 mole) of **12** in 150 ml of 2-propanol. The mixture was heated to 70° and 15 ml of formic acid was added dropwise. After the addition was complete, the mixture was refluxed for 15 minutes and filtered through Celite. The filtrate was made basic with 10% sodium hydroxide and the resulting crystals were removed by filtration, washed with water and dried *in vacuo* to give 18.1 g (91%) of **17**, mp 170-172°. Spectra were identical to the previously prepared sample.

3-(α-Amino)acylindoles (Table IV), Method H (**17**, **18**, **19**, **21**, **22**).

(1-Methyl-1*H*-indol-3-yl)aminocyclopentylmethanone Hydrochloride (**22**).

A solution of 98.0 g (0.36 mole) of **16** in 1l of methanol was treated with 1.0 g of 20% palladium on carbon and shaken in a hydrogen atmosphere (1 atmosphere) for eight hours. The mixture was filtered through Celite and the filtrate concentrated. The residue was partitioned between ether/1.0*N* sodium hydroxide and the basic water layer was reextracted with ether. The combined ether layers were washed with water, dried and concentrated. The residue was crystallized by the addition of petroleum ether to give 82.1 g (85%) of **22**, mp 89-90°. A sample was converted to the hydrochloride salt, mp 273-275°; ir (potassium bromide): 3140 (broad), 1638, 1520 cm^{-1}; nmr (deuterium oxide): δ 2.17-2.78 (m, 8H), 3.88 (s, 3H), 4.78 (HDO + exchangeable protons), 7.37-7.48 (m, 3H), 8.01 (s, 1H), 8.30 (m, 1H).

Anal. Calcd. for $C_{15}H_{18}N_2O \cdot HCl$: C, 64.62; H, 6.87; N, 10.05. Found: C, 64.74; H, 6.96; N, 10.15.

3-(α-Amino)acylindoles (Table IV), Method J (**20**).

2-Amino-2-methyl-1-[(2-propenyl)-1*H*-indol-3-yl]-1-propanone Hydrochloride (**20**).

To a suspension of 4.6 g (0.105 mole) of 54.4% sodium hydride in mineral oil and 100 ml of dimethylsulfoxide was added a solution of 20.2 g (0.1 mole) of **17** in 50 ml of dimethylsulfoxide maintaining the temperature below 25°. When the addition was complete, the reaction mixture was heated to 40° for one hour, cooled to 20° and treated dropwise with 8.0 g (0.105 mole) of 2-propenyl chloride maintaining the temperature below 35°. After the addition was complete, the reaction was stirred at 40° for one hour, diluted with 1.5 l of ice water and extracted with ether (2 x 600 ml). The combined ether extracts were washed copiously with water, dried and concentrated and the residue converted to the hydrochloride salt using 2-propanolic hydrogen chloride to give 22 g (79%) of **20**, mp 283-284°; ir (potassium bromide): 3450 (broad), 1640, 1522 cm^{-1}; nmr (deuterium oxide): δ 2.28 (s, 6H), 4.95 (m, 2H), 5.27 (HDO), 5.49 (m, 2H), 6.22 (m, 1H), 7.44 (m, 3H), 8.54 (m, 1H), 8.68 (s, 1H).

Anal. Calcd. for $C_{15}H_{18}N_2O \cdot HCl$: C, 64.62; H, 6.87; N, 10.05. Found: C, 64.59; H, 6.72; N, 10.10.

(Indol-3-yl)(Substituted-α-amino)ketones (Table IV), Method I (**23 28**, **31-33**).

2-(Ethylamino)-2-methyl-(1-ethyl-1*H*-indol-3-yl)-1-propanone Hydrochloride (**28**).

To a solution of 21.0 g (0.09 mole) of **19** and 16.0 g (0.1 mole) of ethyl iodide in 300 ml of acetone was added 69 g (0.5 mole) of powdered potassium carbonate. The mixture was stirred at reflux for 18 hours, the solids were removed by filtration and the filtrate concentrated. The residue was dissolved in ether, washed with water and the ether layer was extracted with 1.0*M* hydrochloric acid (2 x 200 ml-0.4 mole). The combin-

ed aqueous acid layers were washed with ether (2 x 200 ml), made basic with 10% sodium hydroxide and extracted with ether (3 x 300 ml). The combined ether layers were washed with water, dried, concentrated and converted to the hydrochloride salt using 2-propanolic hydrogen chloride to give 18 g (67%) of **28**, mp 290-292°; ir (potassium bromide): 3463 (broad), 1622 and 1524 cm^{-1}; nmr (deuterium oxide): δ 1.68 (t, 3H), 1.72 (t, 3H), 2.08 (s, 6H), 3.25 (q, 2H), 4.38 (q, 2H), 5.05 (HDO), 7.30-7.58 (m, 3H), 8.44 (m, 1H), 8.53 (s, 1H).

Anal. Calcd. for $C_{16}H_{22}N_2O \cdot HCl$: C, 65.18; H, 7.86; N, 9.50. Found: C, 64.98; H, 7.91; N, 9.33.

(Indol-3-yl)(Substituted-2-amino)ketones (Table IV), Method J (**29**, **30**).

2-(Dimethylamino)-2-methyl-[1-(2-propenyl)-1*H*-indol-3-yl]-1-propanone (**29**).

To a suspension of 6.4 g (0.16 mole) of 60.2% sodium hydride in mineral oil and 100 ml of dimethylsulfoxide was added a solution of 34 g (0.15 mole) of **23** in 100 ml of dimethylsulfoxide keeping the temperature below 25°. When the addition was complete, the mixture was heated at 40° for one hour, cooled to 20° and treated dropwise with 13.1 g (0.17 mole) of 2-propenyl chloride keeping the temperature below 35°. The reaction was stirred at 40° for one hour, diluted with 1.5 l of ice water and extracted with ether (3 x 500 ml). The combined ether layers were washed with water, dried, and concentrated. The residue was converted to the hydrochloride salt using 2-propanolic hydrogen chloride to give 35 g (78%) of **29**, mp 258-260°; ir (potassium bromide): 3438 (broad), 1637, 1527 cm^{-1}; nmr (deuterium oxide): δ 2.12 (s, 6H), 3.18 (s, 6H), 4.98 (m, 2H), 5.15 (HDO + exchangeable protons), 5.50 (m, 2H), 6.21 (m, 1H), 7.42 (m, 3H), 8.48 (m, 1H), 8.63 (s, 1H).

Anal. Calcd. for $C_{17}H_{22}N_2O \cdot HCl$: C, 66.54; H, 7.56; N, 9.13. Found: C, 66.67; H, 7.42; N, 9.07.

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[8] A manuscript involving rearrangements invoking this highly ionic intermediate is in preparation.

[9] In summary of experimental methods: [a] Method F - Iron in aqueous ethanol with a catalytic amount of hydrochloric acid; [b] Method G - The decomposition of formic acid with 5% palladium on carbon in aqueous 2-propanol; [c] Method H - Hydrogen in methanol using 20% palladium on carbon (Pearlman's catalyst).

[10] This exact sequence of reactions has recently been used to prepare a series of simple α-aminoacetophenones. See *J. Org. Chem.*, **51**, 3374 (1986).

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