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8-ARYL-2-AZABICYCLO[3.3.1]NONAN-7-ONES.[1] SYNTHESIS AND RETRO-MICHAEL RING OPENING

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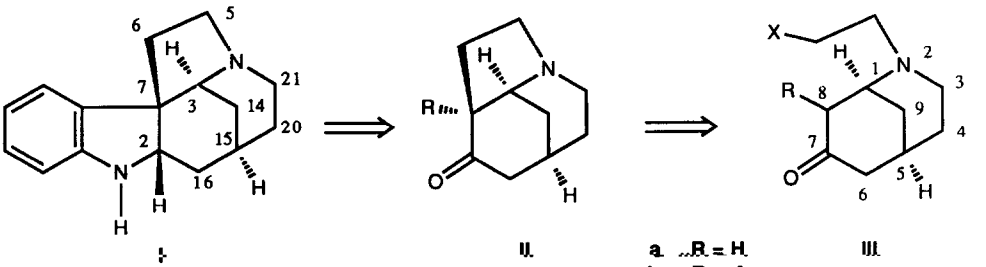
Abstract The synthesis of 8-aryl-2-azabicyclo[3 3 1]nonan-7-ones (**7**) by acid cyclization of 4-(3-aryl-2-oxopropyl)-2-piperidinecarbonitriles (**5**) is reported Bicyclic α-aril-β-amino ketones 7 easily undergo a retro-Michael ring opening to give the corresponding 2-arylcyclohexenones **8**

In the context of our studies on the synthesis of pentacyclic *Strychnos* indole alkaloids,[2] in a previous paper we reported[3] that Fischer indolization of the tricyclic ketone **IIa** takes place upon the methylene α-carbon to give an unnatural pentacyclic structure The regioisomeric pentacyclic *Strychnos*-type system **I** was not obtained At this point, an appropriately arylated tricyclic ketone **IIb**, in which the crucial aryl-C_7 bond[4] would have been previously formed, emerged as a key intermediate for our purpose This ketone would be synthesized from a suitable 8-aryl-2-azabicyclo[3 3 1]nonan-7-one **IIIb** in a way similar to that previously employed for the synthesis of **IIa**[3] (Scheme 1)



Scheme 1

With this goal in mind we have recently reported[5] the preparation of α-(*o*-nitrophenyl)ketone **7a** *via* the sequence **1a→2a→3a→5a→7a** outlined in Scheme 2, in which the key step was the acid-promoted cyclization of a 4-acetonyl-2-piperidinecarbonitrile derivative [6]

Results and Discussion

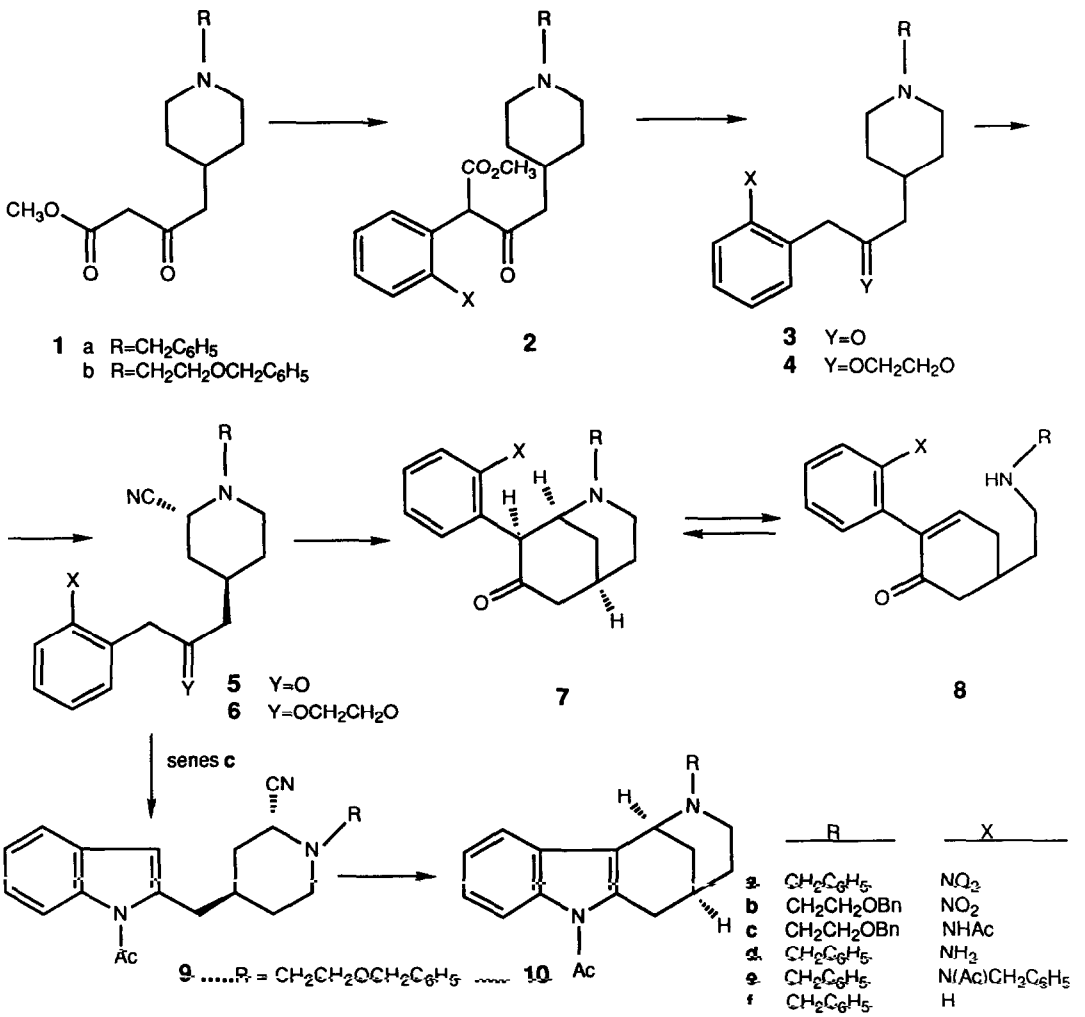
The synthesis of azabicyclo **7b**, in which the substituent at the piperidine nitrogen has the two-carbon chain required for further elaboration of the pyrrolidine ring, was planned as an extension of that previously described for **7a** [5] Thus, β-keto ester **1b**[3] was arylated with *o*-fluoronitrobenzene in the presence of sodium hydride and HMPA,[7] and the resulting β-keto ester **2b**, which appeared to be mainly enolic, was decarbalkoxylated to acetonylpiperidine **3b** with wet DMSO and lithium chloride [8] The modified Polonovski-Potier reaction conditions[9] converted **3b** to 2-cyanopiperidine **5b** However, surprisingly, treatment of **5b** under a variety of acidic conditions (*p*-toluenesulfonic acid, acetic acid, or silver tetrafluoroborate) afforded cyclohexenone **8b** in aproximately 50% yield The expected 2-azabicyclo[3 3 1]nonane (morphan) **7b** was not obtained Formation of **8b** can be accounted for by considering a retro-Michael ring opening from the initially formed 8-arylmorphan **7b** (an α-aryl-β-amino ketone) [10] Attempts to trap **7b** as the corresponding ethylene acetal by treatment of cyclohexenone **8b** with ethylene glycol and *p*-toluenesulfonic acid in refluxing benzene were unsuccessful Acid cyclization (TsOH or HCl, benzene)[11] of acetal **6b**, prepared through the sequence **3b**→**4b**→**6b**, also failed [12]

These results prompted us to reinvestigate the cyclization of **5a** [5] An accurate purification and analysis of the reaction mixture showed that, when the product is isolated as a solid, it is the reported bicyclic ketone **7a** However, when the product is obtained as an oil, its structure corresponds to that of the open compound **8a** The process is reversible Thus, on standing at -20°C, the oil (**8a**) solidifies to give **7a**, whereas a solution of **7a** in chloroform is quantitatively converted in a few hours to the retro-Michael product **8a** [13]

Attempts to obtain the cyclized product **7b** in a similar way were unsuccessful, probably due to the greater lipophilicity of the *N*-substituent, which prevents crystallization

In order to investigate if the electron-withdrawing substituent at the aromatic ring was responsible, at least in part, for the observed fragmentation, we decided to develop a similar synthetic sequence to 8-arylmorphans in which the X substituent were a protected amino group such as acetamido, which would also be useful for our synthetic purpose Nitrile **5c**, required for the cyclization step, was prepared from piperidine **4b**, by catalytic hydrogenation using acetic anhydride as the solvent, followed by deprotection of the acetal function and, finally, cyanation of the resulting piperidine **3c** [14] However, when nitrile **5c** was subjected to the usual cyclization conditions, tetracycle **10**, instead of the expected bicyclo **7c**, was obtained in 40% yield Under milder conditions, 4-(indolylmethyl)-2-cyanopiperidine **9** was also isolated The above results make evident that indolization by interaction of acetamido and ketone groups is faster than the expected cyclization to **7c** and that the resulting intermediate **9** undergoes further cyclization, by way of an iminium cation, to **10** [15]

To avoid the undesired indolization, cyclization was then effected from the disubstituted aniline nitrile **5e**, which was prepared *via* the reaction sequence **4a**→**4d**→**3e**→**5e** (see Experimental Section) However, treatment of cyanopiperidine **5e** with *p*-toluenesulfonic acid gave again a cyclohexenone derivative, **8e**, coming from a retro-Michael ring opening from the initially formed 8-arylmorphan **7e** As in the series **a**, a sample of **8e** solidified on standing at -20°C to give



Scheme 2

the expected bicyclo **7e** When cyclization of **5e** was attempted with formic acid, a mixture of cyclohexenone **8e** and piperidine **3e**, formed by reduction of the initially formed iminium salt, was obtained

A rather similar result was obtained in the unsubstituted aryl series (series **f**, X = H) The required cyanopiperidine **5f** was prepared in the usual way from the corresponding piperidine **3f** which, in turn, was satisfactorily obtained by two alternative ways, either by reductive deamination of **4d** or by direct phenylation[16] of **1a** followed by decarbalkoxylation of the resulting β-keto ester **2f** Acid cyclization of **5f** gave a mixture of arylmorphan **7f** and cyclohexenone **8f** (4 1 ratio), from which **7f** could be separated in a pure form by column chromatography However, **7f** undergone again ring opening in methylene chloride solution to give **8f**, although in this case the conversion

Table 1. Significant ^{13}C Chemical Shifts[a] of Piperidine Derivatives (2-6)

	2b[b]	2f[c]	3b	3c	3e	3f	4a	4b	4d	5b	5c	5e	5f	6b
2-C	53 9	53 3	54 0	54 1	52 6	54 0	53 7	54 2	53 7	52 8	52 6	51 4	51 4	52 9
3-C	31 5	31 2	32 0	31 9	31 0	32 4	33 2	33 1	33 2	34 2	33 9	33 9	33 8	35 3
4-C	33 2	31 6	31 4	31 5	30 7	32 0	31 4	31 2	31 4	27 9	27 6	27 9	27 8	27 5
5-C	31 9	31 2	32 0	31 9	31 0	32 4	33 2	32 7	33 2	31 2	30 8	31 0	30 8	32 3
6-C	54 1	53 3	54 0	54 1	52 6	54 0	53 7	54 2	53 7	48 2	49 1	48 9	48 8	49 6
NCH_2	58 0	63 2	58 1	58 3	62 4	63 9	63 4	58 1	63 3	55 4	55 2	60 1	59 9	55 3
CH_2O	67 6	—	67 7	67 8	—	—	—	67 6	—	67 6	67 4	—	—	67 4
OCH_2Ar	73 1	—	73 1	73 4	—	—	—	72 9	—	73 0	73 0	—	—	73 0
CN	—	—	—	—	—	—	—	—	—	116 5	116 6	116 4	116 2	117 2
Cα[d]	39 5	46 9	49 3	47 8	48 6	48 9	39 8	39 8	40 9	48 6	47 2	48 4	47 3	40 2
Cβ	171 7	202 8	204 7	211 1	206 0	208 6	111 2	111 2	113 1	203 8	209 5	205 5	206 6	111 0
Cγ	101 6	65 0	48 4	49 6	44 0	51 3	44 6	44 5	44 6	49 4	48 3	44 4	50 2	44 0
Ar-X	149 5	130 2	149 0	138 8	140 7	130 1	152 0	151 5	146 2	149 0	139 2	141 3	129 1	151 8
Other	174 5[e]	171 0[e]		169 4[f]	170 4[f]		64 9[g]	64 9[g]	65 0[g]		169 6[f]	171 2[f]		65 19
	51 9	52 5		24 6	51 5						24 2	52 2		65 2
					21 5							22 2		

[a] The δ values are in ppm downfield from Me_4Si The spectra are from $CDCl_3$ solutions [b] Enol form Minor signals due to the carbonyl tautomer were also observed [c] Minor signals due to the enol form were also observed [d] Cα, Cβ, Cγ refer to carbon atoms of the C-4 chain [e] Signals due to CO_2Me [f] Signals due to X [g] Signals due to OCH_2CH_2O

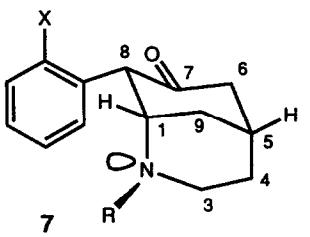
was not complete Interestingly, attempts to characterize arylmorphan **7f** as hydrochloride resulted in the formation of cyclohexenone **8f** hydrochloride

Bicyclic ketones **7** can be easily distinguished from their open α,β-unsaturated isomers **8** by their NMR data, in particular by the ^{13}C signals corresponding to the three aliphatic methine carbons as compared with only one aliphatic methine carbon at δ ~33 for **8** Furthermore, the chemical shift of the carbonyl carbon clearly differentiates both isomers The most significant ^{13}C chemical shifts of arylmorphans **7** and cyclohexenones **8** are listed in Table 2 The absence of a shielding effect upon C-6 in 8-arylmorphans **7**, as compared with the corresponding 8-unsubstituted derivative **11**[17], clearly establishes that the aryl substituent is equatorial Moreover, the upfield chemical shift for C-3 (~2 ppm), C-4 and C-9 (both ~4 ppm) for **7a** and **7e** as compared with **11** is indicative of a conformational change on the nitrogen, the *N*-benzyl group being axially oriented to relieve the steric crowding with the equatorial aryl group at C-8 [18] The data of morphan **7f** suggest an equilibrium between the two conformational arrangements of the piperidine nitrogen

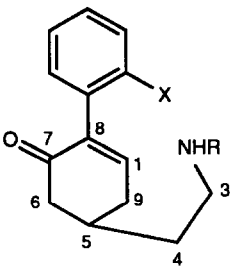
In conclusion, 8-*aryl*-2-azabicyclo[3 3 1]nonan-7-ones easily undergo a retro-Michael reaction, which limits their usefulness in synthesis This behavior contrasts with that of 8-*alkyl*-2-

azabicyclo[3 3 1]nonan-7-ones,[18] which have shown to be stable, and could be accounted for by considering the greater acidity of the methine proton at C-8 in the 8-aryl substituted series and/ or the steric crowding between the bulky equatorial C-8 aryl group and the piperidine nitrogen substituent [19]

Table 2. Significant ^{13}C Chemical Shifts[a] of 8-Aryl-2-azabicyclo[3.3.1]nonan-7-ones (7) and Cyclohexenones (8)



7



8[b]

	7a	7e	7f	11[c]	8a	8b	8e	8f
1-C	60 5	59 1	60 2	53 9	145 7	145 6	148 7	147 2
3-C	42 6	42 8	44 6	44 7	44 5	44 3	44 4	44 9
4-C	27 2	26 6	28 2	31 1	35 8	34 8	35 1	34 6
5-C	30 2	30 0	28 4	28 7	33 1	32 9	33 6	32 9
6-C	46 6	46 2	47 0	47 1	46 4	46 6	45 9	45 5
7-C	208 0	209 7	213 2	211 5	196 4	196 1	198 1	198 1
8-C	56 0	55 5	52 3	40 1	131 5	131 7	130 3	130 6
9-C	28 8	27 5	31 0	33 0	32 7	32 5	32 5	32 6
NCH_2	58 5	57 9	59 4	59 5	54 0	48 8	53 5	53 9
Other			172 2[d]			73 2[e]	171 3[d]	
			53 0			68 5	51 6	
			22 2				22 5	

[a] The δ values are in ppm downfield from Me_4Si The spectra are from $CDCl_3$ solutions [b] For clarity, the numbering system of the morphan nucleus is maintained [c] 11 2-Benzyl-2-azabicyclo[3 3 1]nonan-7-one (data from reference 17) [d] Signals due to $N(Ac)CH_2$ [e] Signals due to CH_2OCH_2

Experimental Section

General. ^1H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ on a Varian XL-200 or Gemini 200 spectrometers Chemical shifts are expressed in parts per million (δ) relative to internal TMS IR spectra were recorded on a Perkin-Elmer 1430 spectrophotometer and only noteworthy absorptions (reciprocal centimeters) are listed Flash chromatography was carried out on SiO_2 (silica gel 60, 230-400 mesh, SDS) TLC was performed on SiO_2 (silica gel G/UV254, Macherey-Nagel), using 95 5 methylene chloride-methanol as

developing solvent, and the spots were located with UV light or iodoplatinate reagent Melting points were determined in a capillary tube on a CTP-MP 300 hotplate apparatus Prior to concentration under reduced pressure, all organic extracts were dried over anhydrous sodium sulfate powder Microanalyses were performed on a Carlo Erba 1106 analyzer by C I D (CSIC), Barcelona

Methyl 1-(2-Benzyloxyethyl)-α-(*o*-nitrophenyl)-4-piperidineacetoacetate (2b) To a suspension of sodium hydride (55%, 3 88 g, 88 8 mmol), previously washed with petroleum ether, in HMPA (120 ml) maintained under nitrogen atmosphere was slowly added β-keto ester **1b**[3] (14 8 g, 44 4 mmol) The reaction mixture was warmed at 60-70°C, *o*-fluoronitrobenzene (5 6 ml, 53 3 mmol) was dropwise added, and the stirring was maintained for 3 h After cooling, the reaction mixture was poured into brine and extracted with methylene chloride The organic extracts were washed with brine, dried, and evaporated The residue was dissolved in ether and exhaustively washed with brine The organic phase was dried and evaporated Flash chromatography (increase from 0% to 10% methanol-methylene chloride) gave pure arylated β-keto ester **2b** (11 3 g, 56%) IR (NaCl) 1650 (enol ester), 1610 (C=C), 1520 and 1345 (NO_2), ^{1}H-NMR 1 0-1 3 (m, 2H, 3- and 5-Hax), 1 55-2 05 (m, 7H), 2 56 (t, J = 6 Hz, 2H, NCH_2), 2 85 (m, 2H, 2- and 6-Heq), 3 54 (t, J = 6 Hz, 2H, OCH_2), 3 64 (s, 3H, OCH_3), 4 50 (s, 2H, OCH_2Ar), 7 26-7 59 (m, 8H, ArH), 8 03 (dd, J = 8 and 1 5 Hz, 1H, 3'-H), 13 0 (br, 1H, OH), (Found C, 65 05, H, 6 90, N, 5 96 Calcd for $C_{25}H_{30}N_2O_6$ 1/2H_2O C, 64 77, H, 6 74 N, 6 04)

Methyl 1-Benzyl-α-(*o*-nitrophenyl)-4-piperidineacetoacetate (2a) Operating as above, from β-keto ester **1a**[3] on a 52 mmol scale, the previously described arylated derivative **2a**[5] was obtained in 55% yield

1-(2-Benzyloxyethyl)-4-[3-(*o*-nitrophenyl)-2-oxopropyl]piperidine (3b) A mixture of β-keto ester **2b** (7 73 g, 17 mmol), lithium chloride (0 79 g, 19 mmol), water (0 61 ml, 34 mmol), and DMSO (55 ml) was heated at 155-160°C for 3 h The suspension was cooled, diluted with ether, and exhaustively washed with brine The organic phase was evaporated to give 5 78 g (85%) of ketone **3b**, which was used without further purification in the next step An analytical sample was obtained by flash chromatography (increase from 1% to 5% methanol in methylene chloride) as an oil IR ($CHCl_3$) 1710 (CO), 1520 and 1345 (NO_2), ^{1}H-NMR 1 37 (qd, J = 12 and 3 Hz, 2H, 3- and 5-Hax), 1 74 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 1 93 (m, 1H, 4-Hax), 2 08 (t, J =12 Hz, 2H, 2- and 6-Hax), 2 55 (d, J = 6 5 Hz, 2H, CH_2CO), 2 64 (t, J =6 Hz, 2H, NCH_2), 2 95 (dm, J =12 Hz, 2H, 2- and 6-Heq), 3 62 (t, J = 6 Hz, CH_2O), 4 11 (s, 2H, $ArCH_2CO$), 4 56 (s, 2H, OCH_2Ar), 7 29-7 38 (m, 6H, ArH), 7 46 (t, J = 8 Hz, 1H, 4'-H), 7 61 (t, J = 8 Hz, 1H, 5'-H), 8 12 (d, J = 8 Hz, 1H, 3'-H), (Found C, 67 86, H, 7 09, N, 6 57 Calcd, for $C_{23}H_{28}N_2O_4$ 1/2H_2O C, 68 12, H, 7 20, N, 6 90)

***trans*-1-(2-Benzyloxyethyl)-4-[3-(*o*-nitrophenyl)-2-oxopropyl]-2-piperidinecarbonitrile (5b)** A solution of *m*-chloroperbenzoic acid (85%, 1 76 g, 8 7 mmol) in anhydrous methylene chloride (40 ml) was added over 15 min to a stirred solution of ketone **3b** (3,12 g, 7 9 mmol) in anhydrous methylene chloride (40 ml) maintained at 0°C under argon atmosphere Stirring was continued at 0°C for one hour After the resulting solution had been cooled at -15°C, trifluoroacetic anhydride (4 40 ml, 31 6 mmol) was added dropwise and the mixture was stirred at -15°C for 1 h and at room temperature for 15 min Potassium cyanide (2 05 g, 31 6 mmol) in water (20 ml) was then added and the pH adjusted to 5 by the addition of solid sodium acetate The two phase mixture was vigorously stirred for 30 min, basified with 10% aqueous sodium carbonate, and extracted with methylene chloride The organic extracts were washed with water, dried, and evaporated Flash chromatography (increase from 0 to 2% methanol-methylene chloride) gave nitrile **5b** (2 65 g, 80%) An analytical sample was obtained by crystallization (ether-acetone) mp 81-82°C, IR (NaCl) 1710 (CO), 1520 and 1350 (NO_2), ^{1}H-NMR 1 32 (qd, J = 12 and 4 5Hz, 1H, 5-Hax), 1 58 (td, J = 12 and 4 5 Hz, 1H, 3-Hax), 1 76 (dm, J = 12 Hz, 1H, 5-Heq), 1 96 (dm, J = 12 Hz, 3-Heq), 2 25 (m, 1H, 4-Hax), 2 45 (td, J = 12 and 2 5 Hz, 1H, 6-Hax), 2 55 (d, J =6 5 Hz, 2H, CH_2CO), 2 72 (AA'XY, 2H, NCH_2), 2 81 (dm, J = 12 Hz, 1H, 6-Heq), 3 57 (AA'XY, 2H, OCH_2), 4 04 (t, J = 3Hz, 1H,

2-Heq), 4 08 (s, 2H, $ArCH_2CO$), 4 53 (s, 2H, OCH_2Ar), 7 24-7 34 (m, 6H, ArH), 7 46 (td, J = 8 and 1 5 Hz, 1H, 4'-H), 7 58 (td, J = 8 and 1 5 Hz, 1H, 5'-H), 8 12 (dd, J = 8 and 1 5 Hz, 1H, 3'-H), (Found C, 67 64, H, 6 56, N, 9 46 Calcd for $C_{24}H_{27}N_3O_4$ 1/3C_3H_6O C, 67 98, H, 6 71, N, 9 32)

Cyclization of Cyanopiperidine 5b A stirred solution of cyanopiperidine **5b** (230 mg, 0 5 mmol) in 50% acetic acid (12 ml) was heated under nitrogen at 90-100°C overnight The resulting solution was cooled, basified with 10% aqueous sodium carbonate solution, and extracted with methylene chloride Drying and evaporation of the organic extracts gave an oil which was purified by flash chromatography (increase from 0% to 10% methanol-methylene chloride) to afford 110 mg (50%) of **5-[2-(2-benzyloxyethylamino)ethyl]-2-(*o*-nitrophenyl)-2-cyclohexenone (8b)** as an oil IR ($CHCl_3$) 1675 (CO), 1520 and 1350 (NO_2), ^{1}H-NMR 2 77 (t, J = 8 Hz, 2H, NCH_2), 2 90 (t, J = 5 Hz, 2H, NCH_2), 3 65 (t, J = 5 Hz, 2H, OCH_2), 4 53 (s, 2H, OCH_2Ar), 6 95 (m, 1H, =CH), 7 26-7 70 (m, 8H, ArH), 8 05 (dd, J = 8 and 1 5 Hz, 3'-H), (Found C, 68 39, H, 6 40, N, 6 71 Calcd for $C_{23}H_{26}N_2O_4$ H_2O C, 68 29, H, 6 97, N, 6 92)

1-Benzyl-4-[2,2-(ethylenedioxy)-3-(*o*-nitrophenyl)propyl]piperidine (4a) A stirred solution of ketone **3a**[5] (5 53 g, 15 7 mmol), *p*-toluenesulfonic acid monohydrate (5 g, 23 9 mmol), and ethylene glycol (47 ml) in anhydrous benzene (300 ml) was refluxed for 24 h with removal of water with a Dean-Stark trap The reaction mixture was poured into saturated aqueous sodium carbonate solution The organic phase was separated and the aqueous layer was extracted with ether The combined organic extracts were washed with saturated aqueous sodium carbonate solution, dried, and evaporated Flash chromatography of the residue (increase from 0% to 5% methanol in methylene chloride) afforded 4 83 g (78%) of ketal **4a** ^{1}H-NMR 1 26 (qd, J = 12 and 2 5 Hz, 3- and 5-Hax), 1 5 (m, 1H, 4-Ha), 1 53 (d, J = 4 Hz, 2H, 4-CH_2), 1 73 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 1 94 (td, J = 12 and 2 5 Hz, 2H, 2- and 6-Hax), 2 82 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 3 26-3 42 and 3 62-3 78 (2m, AA'BB', 2H each, OCH_2CH_2O), 3 38 (s, 2H, CH_2Ar), 3 46 (s, 2H, NCH_2Ar), 7 25-7 45 (m, 8H, ArH), 7 75 (dd, J = 8 and 1 5 Hz, 1H, 3'-H), (Found C, 69 81, H, 7 26, N, 7 23 Calcd for $C_{23}H_{28}N_2O_4$ C, 69 98, H, 7 12 N, 7 07)

1-(2-Benzyloxyethyl)-4-[2,2-(ethylenedioxy)-3-(*o*-nitrophenyl)propyl]piperidine (4b) Operating as above, from ketone **3b** (4 3 g, 10 8 mmol), *p*-toluenesulfonic acid monohydrate (3 4 g, 16 4 mmol), and ethylene glycol (32 ml) in benzene (300 ml), ketal **4b** (3 25 g, 69%) was obtained after flash chromatography (increase from 0% to 15% methanol-methylene chloride) An analytical sample melted at 95-97°C (ether-acetone) ^{1}H-NMR 1 30 (qd, J = 12 and 2 5 Hz, 2H, 3- and 5-Hax), 1 45 (m, 1H, 4-Hax), 1 55 (d, J = 4 Hz, 2H, 4-CH_2), 1 75 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 2 00 (td, J = 12 and 2 5 Hz, 2H, 2- and 6-Hax), 2 60 (t, J = 7 Hz, 2H, NCH_2), 2 90 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 3 30-3 40 and 3 70-3 80 (2m, AA'BB', 2H each, OCH_2CH_2O), 3 40 (s, 2H, CH_2Ar), 3 60 (t, J = 7 Hz, 2H, OCH_2), 4 53 (s, 2H, OCH_2Ar), 7 2-7 4 (m, 8H, ArH), 7 78 (dd, J = 8 and 1 5 Hz, 3'-H), (Found C, 68 01, H, 7 29, N, 6 42 Calcd for $C_{25}H_{32}N_2O_5$ C, 68 18, H, 7 27, N, 6 36)

***trans*-1-Benzyl-4-[2,2-(ethylenedioxy)-3-(*o*-nitrophenyl)propyl]-2-piperidinecarbonitrile (6a)** was prepared from **4a** (1 9 g, 4 8 mmol) as described for **5b**, in 61% yield ^{1}H-NMR 1 26 (m, 1H, 5-Hax), 1 42 (td, J = 12 and 4 5 Hz, 1H, 3-Hax), 1 58 (m, 2H, 4-CH_2), 1 75 (dm, 1H, 5-Heq), 1 84 (m, 1H, 4-Hax), 2 07 (dm, 1H, 3-Heq), 2 43 (td, J = 12 and 2 5 Hz, 1H, 6-Hax), 2 82 (dm, J = 12 Hz, 1H, 6-Heq), 3 39 (s, 2H, CH_2Ar), 3 52 and 3 68 (2d, J = 13 Hz, 1H each, NCH_2Ar), 3 38 and 3 76 (2m, AA'BB' system, 2H each, OCH_2CH_2O), 3 73 (br, 1H, 2-Heq), 7 25-7 50 (m, 8H, ArH), 7 8 (dd, J = 8 and 1 5 Hz, 1H, 3'-H), (Found C, 68 03, H, 6 72, N, 9 53 Calcd for $C_{24}H_{27}N_3O_4$ C, 68 39, H, 6 46, N, 9 97)

***trans*-1-(2-Benzyloxyethyl)-4-[2,2-(ethylenedioxy)-3-(*o*-nitrophenyl)propyl]-2-piperidinecarbonitrile (6b)** was prepared from **4b** (750 mg, 1 7 mmol) as described for **5b**, in 70% yield ^{1}H-NMR 1 20 (qd, J = 12 and 3 Hz, 1H, 5-Hax), 1 45 (td,

J = 12 and 3 Hz, 1H, 3-Hax), 1 50 (d, J = 5Hz, 2H, 4-CH_2), 1 65 (dm, J = 12 Hz, 1H, 5-Heq), 1 75 (m, 1H, 4-Hax), 2 02 (dq, J = 12 and 2 5 Hz, 1H, 3-Heq), 2 32 (td, J = 12 and 3 Hz, 1H, 6-Hax), 2 6 (m, 2H, NCH_2), 2 75 (dm, J = 12 Hz, 1H, 6-Heq), 3 31 (s, 2H, CH_2Ar), 3 49 (m, 4H, OCH_2CH_2O), 3 71 (m, 2H, OCH_2), 3 92 (t, J = 3 Hz, 1H, 2-Heq), 4 45 (s, 2H, OCH_2Ar), 7 26-7 50 (m, 8H, ArH), 7 75 (d, J = 8 Hz, 1H, 3'-H), (Found C, 67 12, H, 6 71, N, 8 61 Calcd for $C_{26}H_{31}N_3O_5$ C, 67 07, H, 6 72 N, 9 03)

4-[3-(*o*-Acetamidophenyl)-2-oxopropyl]-1-(2-benzyloxyethyl)piperidine (3c) A solution of ketal **4b** (3 07 g, 7 0 mmol) in acetic anhydride (100 ml) was hydrogenated at room temperature and atmospheric pressure over 10% palladium on charcoal (1 25 g) until the required volume of hydrogen was absorbed The mixture was poured into ice-water (190 ml) and the two phase mixture was stirred until it became homogeneous At this point, 12N hydrochloric acid (8 5 ml) was dropwise added, and the stirring was maintained for 45 min The catalyst was removed by filtration and washed with water The resulting solution was cooled, basified with cold 2N aqueous sodium hydroxide, and extracted with methylene chloride The organic phase was dried and evaporated Flash chromatography of the residue (increase from 0 to 15% methanol-methylene chloride) afforded 1 86 g (65%) of acetamide 3c An analytical sample was obtained by recrystallization from ether mp 65-67°C, IR ($CHCl_3$) 1670-1705 (CO), ^{1}H-NMR 1 25 (qd, J = 12 and 2 5 Hz, 2H, 3- and 5-Hax), 1 57 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 1 8 (m, 1H, 4-Hax), 2 00 (td, J = 12 and 2 5 Hz, 2H, 2- and 6-Hax), 2 21 (s, 3H, CH_3), 2 51 (d, J = 7 Hz, 2H, 4-CH_2), 2 59 (t, J = 6 Hz, 2H, NCH_2), 2 90 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 3 57 (t, J = 6 Hz, 2H, OCH_2), 3 68 (s, 2H, CH_2Ar), 7 10 (td, J = 8 and 1 5 Hz, 1H, 4'-H), 7 15 (dt, J = 8 and 1 5 Hz, 1H, 6-H), 7 25-7 45 (m, 6H, ArH), 7 9 (d, J = 8 Hz, 1H, 3'-H), 8 6 (br s, 1H, NH), (Found C, 73 59, H, 7 98, N, 6 94 Calcd for $C_{25}H_{32}N_2O_3$ C, 73 59, H, 7 91, N, 6 87)

***trans*-4-[3-(*o*-Acetamidophenyl)-2-oxopropyl]-1-(2-benzyloxyethyl)-2-piperidinecarbonitrile (5c)** By use of a procedure identical to the one described for the preparation of **5b**, piperidine **3c** (720 mg, 1 9 mmol) was converted into the title nitrile The crude product was purified by flash chromatography (increase from 0 to 10% methanol-methylene chloride) to give **5c** (500 mg, 62%) as an oil IR ($CHCl_3$) 1665-1705 (CO), ^{1}H-NMR 1 22 (dq, J = 12 and 4 5 Hz, 1H, 5-Hax), 1 50 (td, J = 12 and 4 5 Hz, 1H, 3-Hax), 1 65 (dm, J = 12 Hz, 1H, 5-Heq), 1 85 (dm, J =12 Hz, 1H, 3-Heq), 2 12 (m, 1H, 4-Hax), 2 24 (s, 3H, CH_3), 2 40 (td, J = 12 and 2 5 Hz, 1H, 6-Hax), 2 50 (d, J = 6 5 Hz, 2H, 4-CH_2), 2 71 (AA'XY system, 2H, NCH_2), 2 8 (dm, J = 12 Hz, 1H, 6-Heq), 3 56 (td, AA'XY, 2H, OCH_2), 3 67 (s, 2H, CH_2Ar), 4 01 (t, J = 3 Hz, 1H, 2-Heq), 4 55 (s, 2H, OCH_2Ar), 7 13 (td, J = 8 and 1 5 Hz, 1H, 4'-H), 7 18 (td, J = 8 and 1 5 Hz, 1H, 6'-H), 7 24-7 40 (m, 6H, ArH and 5'-H), 7 87 (d, J = 8 Hz, 1H, 3'-H), 8 57 (br s, 1H, NH), (Found C, 71 86, H, 7 25, N, 9 59 Calcd for $C_{26}H_{31}N_3O_3$ C, 72 06, H, 7 16, N, 9 70)

Cyclization of Cyanopiperidine 5c

a) A solution of amino nitrile **5c** (110 mg, 0 25 mmol) and anhydrous *p*-toluenesulfonic acid (86 mg, 0 5 mmol) in benzene (25 ml) was refluxed under argon overnight, using a Dean-Stark apparatus The mixture was cooled and basified with 10% aqueous sodium carbonate solution The organic layer was separated and the aqueous one was extracted with methylene chloride The combined organic extracts were washed with brine, dried, and evaporated Flash chromatography (increase from 0% to 5% methanol-methylene chloride) afforded **7-acetyl-2-(2-benzyloxyethyl)-1,2,3,4,5,6-hexahydro-1,5-methanoazocino[4,3-*b*]indole (10**, 39 mg, 40%) IR ($CHCl_3$) 1690 (CO), ^{1}H-NMR 2 65 (s, 3H, $COCH_3$), 2 94 (m, 2H, NCH_2), 3 15 (dd, J =17 and 6 Hz, 1H, 6-H), 3 57 (m, 2H, OCH_2), 4 19 (t, J = 2 Hz, 1H, 1-H), 4 46 (s, 2H, OCH_2Ar), 7 13-7 50 (m, 8H, ArH), 7 90 (d, J = 8 Hz, 1H, 8-H), ^{13}C-NMR 24 6 (5-C), 26 6 (CH_3), 30 8, 31 8, and 32 2 (4-, 6-, and 12-C), 44 0 (3-C), 50 2 (1-C), 55 5 (NCH_2), 67 5 (CH_2O), 72 4 (OCH_2Ar), 114 4-138 1 (Ar), 169 5 (CO)

b) Operating as above, but shortening the reaction time to 4 h, from 160 mg (0 37 mmol) of **5c**, ***trans*-1-acetyl-2-[1-(2-benzyloxyethyl)-2-cyano-4-piperidylmethyl]indole (9**, 54 mg, 35%) was obtained after flash chromatography (methylene chloride) Further elution with 3-5% methanol in methylene chloride afforded azocinoindole **10** (34 mg, 23%) Compound **9** ^{1}H-

NMR (60 MHz) 2 6 (s, 3H, $COCH_3$), 2 85 (d, J = 7 Hz, 2H, 4-CH_2), 3 6 (br, 1H, 2-Heq), 4 3 (s, 2H, OCH_2Ar), 6 1 (s, 1H, 3-H indole), 7 0 (s, 5H, ArH), ^{13}C-NMR 27 7 (CH_3), 27 7 (4-C), 31 5 (4-CH_2), 32 5 (5-C), 36 6 (3-C), 49 7 (6-C), 53 0 (2-C), 55 4 (NCH_2), 67 5 (CH_2O), 73 0 (OCH_2Ar), 109 8 (3-In), 110 4 (7-In), 114 3 (CN), 120 4 (4-In), 123 0 (5-In), 123 6 (6-In), 127 6, 127 7, 128 4 (*o*-, *m*-, *p*-C_6H_5), 129 8 (3a-In), 136 0 (2-In), 139 0 (ipso-C_6H_5), 140 0 (7a-In), 170 0 (CO)

4-[3-(*o*-Aminophenyl)-2,2-(ethylenedioxy)propyl]-1-benzylpiperidine (4d) A solution of nitro acetal **4a** (2 6 g, 6 5 mmol) in absolute ethanol (100 ml) was hydrogenated at atmospheric pressure in the presence of 10% palladium on charcoal (565 mg) until the required volume of hydrogen was absorbed After filtration through Celite and removal of the solvent, a yellow foam was obtained Purification by flash chromatography (98 2 methylene chloride-methanol) afforded aniline **4d** (1 55 g, 65%) ^{1}H-NMR 1 32 (qd, J = 12 and 3 Hz, 2H, 3- and 5-Hax), 1 55 (m, 1H, 4-Hax), 1 64 (d, J = 5 Hz, 4-CH_2), 1 78 (dm, J = 12 Hz, 3- and 5-Heq), 1 97 (td, J = 12 and 1 8 Hz, 2H, 2- and 6-Hax), 2 85 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 2 92 (s, 2H, CH_2Ar), 3 48 (s, 2H, NCH_2Ar), 3 56-3 77 (2m, AA'BB', 2H each, OCH_2CH_2O), 4 15 (br s, 2H, NH_2), 6 64 (d, J = 7 Hz, 1H, 3'-ArH), 6 70 (t, J = 7 Hz, 1H, 5'-ArH), 7 03 (t, J = 7 Hz, 1H, 4'-ArH), 7 26 (d, J = 7 Hz, 1H, 6'-ArH), 7 30 (s, 5H, ArH), (Found C, 74 45, H, 8 28, N, 7 55 Calcd for $C_{23}H_{30}N_2O_2$ 1/4H_2O C, 74 46, H, 8 28, N, 7 55)

1-Benzyl-4-{3-[o-(*N*-benzylacetamido)phenyl]-2-oxopropyl}piperidine (3e) A solution of aniline **4d** (1 46 g, 4 mmol) and benzyl chloride (0 5 ml, 4 mmol) in absolute ethanol (75 ml) was refluxed for 5 h The solvent was evaporated and the residue was redisolved in methylene chloride and washed with 2N sodium hydroxide solution The organic phase was dried and evaporated to yield an oil which was submitted twice to the same reaction conditions (0 5 ml of benzyl chloride, 75 ml of ethanol, reflux for 5 h) and the same work-up Finally, the resulting crude oil was purified by flash chromatography (increase from 0 to 3% methanol-methylene chloride) to yield the benzylated aniline (1 05 g, 58%)

A solution of this benzylamine (1 15 g, mmol) in acetic anhydride (35 ml) was stirred at room temperature for 5 h Ice-water (70 ml) was then added and the resulting mixture was stirred until it became homogeneous To this cooled mixture, 12N hydrochloric acid (11ml) was added dropwise and the solution was stirred for 45 min The mixture was basified with 2N sodium hydroxide solution and extracted with methylene chloride The organic extracts were dried and evaporated to give a residue which was purified by flash chromatography Elution with 0-5% methanol in methylene chloride afforded 1 04 g (90%) of amido ketone **3e** ^{1}H-NMR 1 25 (qd, J = 12 and 2 5 Hz, 2H, 3- and 5-Hax), 1 65 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 1 75 (s, 3H, CH_3), 1 8 (m, 1H, 4-H), 2 00 (td, J= 12 and 2 5 Hz, 2H, J = 12 and 2 5 Hz, 2H, 2- and 6-Hax), 2 27 (d, J = 6 5 Hz, 2H, 4-CH_2), 2 90 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 3 48 (s, 2H, NCH_2Ar), 3 50 (s, 2H, $COCH_2Ar$), 4 35 and 5 15 (2d, J = 15 Hz, 1H each, $CONCH_2Ar$), 6 5-7 7 (m, 14H, ArH), (Found C, 74 62, H, 7 46, N, 5 62 Calcd for $C_{30}H_{34}N_2O_2$ 2/5CH_2Cl_2 C, 74 73, H, 7 18 N, 5 73)

***trans*-1-Benzyl-4-{3-[*o*-(*N*-benzylacetamido)phenyl]-2-oxopropyl}-2-piperidinecarbonitrile (5e)** was prepared from piperidine **3e** as described above for **5b** The crude product was purified by flash chromatography (increase from 0 to 2% methanol-methylene chloride) to give 766 mg (80%) of the title compound ^{1}H-NMR 1 26 (m, 1H, 5-Hax), 1 46 (td, J = 12 and 4 Hz, 1H, 3-Hax), 1 70 (masked, 5-Heq), 1 75 (s, 3H, CH_3), 1 85 (dm, J = 12 Hz, 1H, 3-Heq), 2 15 (m, 1H, 4-Hax), 2 27 (d, J = 6 Hz, 2H, 4-CH_2), 2 48 (td, J = 12 and 2 Hz, 1H, 6-Hax), 2 83 (dm, J = 12 Hz, 1H, 6-Heq), 3 48 (s, 2H, $COCH_2Ar$), 3 55 and 3 71 (2d, J = 13 Hz, 1H each, NCH_2Ar), 3 76 (br s, 1H, 2-Heq), 4 41 and 5 09 (2d, J = 14 Hz, 1H each, $N(Ac)CH_2Ar$), 6 82 (d, J = 7 5 Hz, 1H, ArH), 7 21-7 33 (m, 13H, ArH), (Found C, 71 04, H, 6 68, N, 7 47 Calcd for $C_{31}H_{33}N_3O_2$ 3/5CH_2Cl_2 C, 70 99, H, 6 45, N, 7 85)

Cyclization of Cyanopiperidine 5e Amino nitrile **5e** (500 mg, 1 04 mmol) was added under argon atmosphere to a solution of *p*-toluenesulfonic acid monohydrate (397 mg, 2 08 mmol) in anhydrous benzene (75 ml), previously refluxed for 3 h using a Dean-

Stark apparatus The mixture was refluxed overnight. The resulting solution was cooled and partitioned between methylene chloride and 10% aqueous sodium carbonate solution The organic phase was washed with brine, dried, and evaporated to give an oil Purification by flash chromatography (increase from 4 to 8% methanol-methylene chloride) gave 198 mg (42%) of **2-[*o*-(*N*-benzylacetamido)phenyl]-5-(2-benzylaminoethyl)-2-cyclohexenone (8e)** ^{1}H-NMR 1 87 (s, 3H, CH_3), 2 72 (t, J = 7 Hz, NCH_2), 3 83 (s, 2H, NCH_2Ar), 3 89 and 5 38 (2d, J = 14 Hz, 1H each, $N(Ac)CH_2Ar$), 6 70-7 50 (m, 15H, =CH and ArH), (Found C 74 36, H, 6 77, N, 5 56 Calcd. for $C_{30}H_{32}N_2O_2$ 1/2CH_2Cl_2 C, 73 99, H, 6 71, N, 5 65)

A pure sample of **8e** partially solidified on standing at -20°C Crystallization from ether afforded the cyclized derivative **(1*RS*,5*SR*,8*RS*)-2-benzyl-8-[*o*-(*N*-benzylacetamido)phenyl]-2-azabicyclo[3.3.1]nonan-7-one (7e)** mp 134-135°C, ^{1}H-NMR 3 05 (ddd, J = 13 5, 13, and 3 Hz, 1H, 3-Hax), 3 56 (d, J = 4Hz, 1H, 8-Hax), 3 58 and 3 71 (2d, J = 14 Hz, 1H each, NCH_2Ar), 4 03 (br s, 1H, 1-H), 4 48 and 4 73 (2d, J = 14 Hz, 1H each, $N(Ac)CH_2Ar$), 6 70-7 60 (m, 14H, ArH), (Found C, 79 68, H, 7 15, N, 6 08 Calcd for $C_{30}H_{32}N_2O_2$ C, 79 61, H, 7 08, N, 6 19)

1-Benzyl-4-(3-phenyl-2-oxopropyl)piperidine (3f)

Method A. From Aniline 4d A cold solution of sodium nitrite (106 mg, 1 54 mmol) in water (0 55 ml) was slowly added to a stirred mixture of aniline **4d** (435 mg, 1 2 mmol) and 6N hydrochloric acid (3 5 ml), cooled at -10°C After 5 min, the resulting cold solution was added dropwise to a stirred aqueous solution of hypophosphorous acid (50%, 8 2 ml) cooled at -10°C The stirring was maintained for 2 h, while the temperature of the reaction mixture was held between -10°C and 0°C The mixture was basified with 10% aqueous sodium carbonate solution and extracted with methylene chloride The extracts were washed with brine, dried, and evaporated The crude product was submitted to acid hydrolysis (3 5 N HCl, room temperature, 2 h) The resulting solution was basified with 2N sodium hydroxide solution, extracted with methylene chloride, dried, and evaporated Flash chromatography of the resulting oil (98 2 methylene chloride-methanol) gave ketone **3f** (280 mg, 77%) IR ($CHCl_3$) 1707 (CO), ^{1}H-NMR 1 18 (qd, J = 12 and 3 Hz, 2H, 3- and 5-Hax), 1 58 (dm, J = 12 5 Hz, 2H, 3- and 5-Heq), 1 82 (m, 1H, 4-Hax), 1 95 (td, J = 12 and 2 5 Hz, 2H, 2- and 6-Hax), 2 35 (d, J = 6 8 Hz, 2H, 4-CH_2), 2 81 (dm, J = 12 Hz, 2H, 2- and 6-Heq), 3 46 (s, 2H, NCH_2Ar), 3 63 (s, 2H, CH_2Ar), 7 15-7 35 (m, 10H, ArH), (Found C, 79 99, H, 8 04, N, 4 36 Calcd for $C_{21}H_{25}NO$ 1/2H_2O C, 79 81, H, 7 97, N, 4 43)

Method B. From β-Keto Ester 2f A solution of β-keto ester **1a** (3g, 10 4 mmol) in anhydrous dimethoxyethane (10 ml) was slowly added under nitrogen to a suspension of sodium hydride (55%, 450 mg, 10 4 mmol), previously washed with hexane, in dimethoxyethane (15 ml) Then, diphenyliodonium chloride (3 39 g, 10 4 mmol) was added dropwise and the resulting mixture was heated at 70°C for 24 h The solvent was evaporated and the residue was partitioned between 1 2 N hydrochloric acid and ether The aqueous phase was basified with ammonium hydroxide until pH 8 and extracted with methylene chloride After evaporation of the solvent, a dark oil was obtained Purification by flash chromatography (increase from 1 to 2 5% methanol-methylene chloride) gave 1 18 g (31%) of **methyl 1-benzyl-α-phenyl-4-piperidineacetoacetate (2f)** ^{1}H-NMR 0 92 (m, 2H, 3- and 5-Hax), 1 33 (dm, J = 12 Hz, 2H, 3- and 5-Heq), 1 65 (m, 1H, 4-Hax), 1 78 (t, J = 11 5 Hz, 2- and 6-Hax), 2 32 (d, J = 6 5 Hz, 2H, 4-CH_2), 2 63 (dm, J = 11 5 Hz, 2- and 6-Heq), 3 33 (s, 2H, NCH_2Ar), 3 35 (s, 1H, CH), 3 63 (s, 3H, OCH_3), 7 17 and 7 23 (2s, 5H each, ArH)

A solution of β-keto ester **2f** (0 65 g, 1 78 mmol) in 3N hydrochloric acid (10 ml) was refluxed for 3 h After cooling the reaction mixture was basified with 2N sodium hydroxide solution and extracted with methylene chloride The extracts were dried and evaporated Flash chromatography (98 2 methylene chloride-methanol) of the residue gave 385 mg (65%) of ketone **3f**

***trans*-1-Benzyl-4-(3-phenyl-2-oxopropyl)-2-piperidinecarbonitrile (5f)** was prepared as reported above for **5b**, 640 mg (2 08 mmol) of piperidine **3f** was treated sequentially with *m*-chloroperbenzoic acid (70%, 565 mg, 2 3 mmol), trifluoroacetic anhydride (1 17 ml, 8 3 mmol), and potassium cyanide (405 mg, 6 25 mmol) After workup and flash chromatography (methylene chloride), cyanopiperidine **5f** (563 mg, 81%) was obtained IR($CHCl_3$) 1713 (CO), ^{1}H-NMR 1 18 (qd, J = 12 and 4 Hz, 1H, 5-Hax), 1 39 (td, J = 12 and 4 Hz, 1H, 3-Hax), 1 70 (dq, J = 13 and 2 5 Hz, 1H, 5-Heq), 1 83 (dq, J = 13 and 3 Hz, 1H, 3-Heq), 2 18 (m, 1H,

4-Hax), 2 37 (d, J = 7 5 Hz, 2H, 4-CH_2), 2 45 (tm, J = 12 Hz, 1H, 6-Hax), 2 80 (dm, J = 12 Hz, 1H, 6-Heq), 3 52 and 3 68 (2d, J = 13 Hz, 1H each, NCH_2Ar), 3 66 (s, 2H, CH_2Ar), 3 71 (br s, 1H, 2-Heq), 7 15-7 40 (m, 10H, ArH), (Found C, 75 78, H, 7 13, N, 7 95 Calcd for $C_{22}H_{24}N_2O$ H_2O C, 75 40, H, 7 47, N, 7 99)

(2*RS*,5*SR*,8*RS*)-2-Benzyl-8-phenyl-2-azabicyclo[3.3.1]nonan-7-one (7f) A solution of 2-cyanopiperidine **5f** (560 mg, 1 68 mmol) in methanol (72 ml) containing 12 N hydrochloric acid (8 ml) was refluxed for 24 h under nitrogen atmosphere Methanol was evaporated and the residue was basified with aqueous sodium carbonate solution and extracted with methylene chloride The evaporation of the extracts left an oil which was purified by flash chromatography (increase 1 to 2% methanol in methylene chloride) to yield azabicyclo **7f** (185 mg, 36%) as an oil IR ($CHCl_3$) 1690 (CO), ^{1}H-NMR 1 59 (dm, J = 13 Hz, 1H, 4-Heq), 1 83 (dm, J = 13 Hz, 1H, 9-Hanti), 1 9 (masked, 1H, 9-Hsyn), 1 98 (tm, J = 13 Hz, 1H, 4-Hax), 2 3-2 8 (m, 5H, 3- and 6-CH_2, 5-H), 3 41 (br s, 1H, 1-H), 3 75 and 3 83 (2d, J = 13 Hz, 1H each, NCH_2Ar), 4 09 (br s, 1H, 8-H), 7 02 (d, J = 8 Hz, 1H, ArH), 7 20-7 37 (m, 9H, ArH) A similar result was obtained when cyclization was effected with *p*-toluenesulfonic acid, as described for **5e** On standing in methylene chloride solution, **7f** was partially converted to cyclohexenone **8f** A sample of **7f** was dissolved in methanol and then treated with hydrogen chloride in methanol Evaporation of solvent and crystallization of the residue from methanol afforded **5-(2-benzylaminoethyl)-2-phenyl-2-cyclohexenone (8f) hydrochloride** mp 236-237°C, ^{1}H-NMR (DMSO-d_6) 1 76 (br s, 2H, 5-CH_2), 2 27-2 58 (m, 5H), 2 97 (br s, 2H, NCH_2), 4 12 (br s, 2H, $ArCH_2N^+$), 7 10 (d, J = 1 Hz, 3-H), 7 27-7 58 (m, 10H, ArH), 9 60 (br, NH_2), ^{13}C-NMR (DMSO-d_6) 31 0 (5-CH_2), 32 1 (4-C), 32 2 (5-C), masked (CH_2N^+), 44 4 (6-C), 50 2 ($ArCH_2N^+$), 132 5 (2-C), 148 4 (3-C), 197 4 (CO), (Found C, 73 72, H, 7 13, N, 4 09 Calcd for $C_{21}H_{23}NO$ HCl C, 73 76, H, 7 07, N, 4 11)

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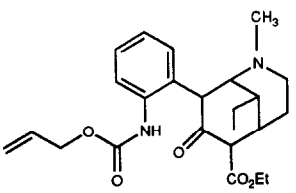

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