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A STEREOSELECTIVE SYNTHESIS OF CIS-4-ACETONYL-1-BENZYL-3-ETHYLPIPERIDINE[1]

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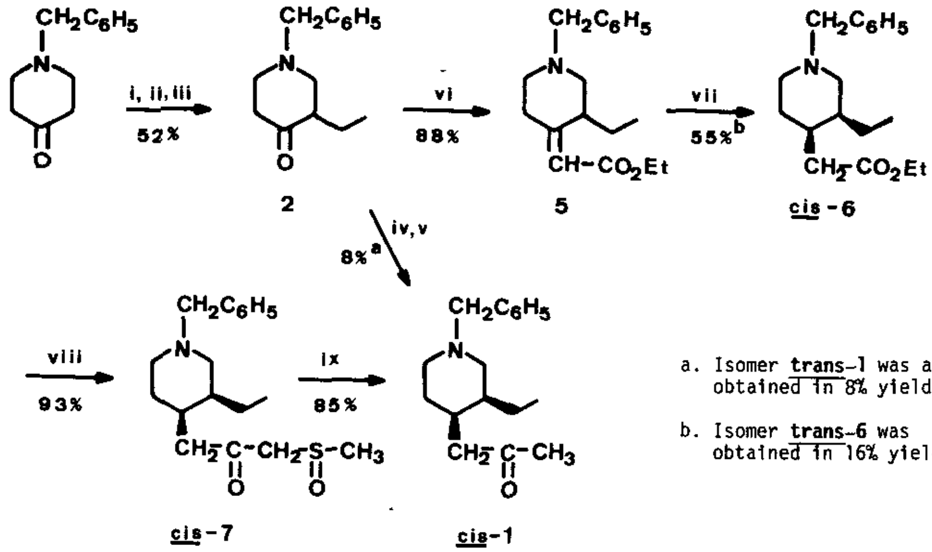
Abstract ——The title compound cis-**1**, a potential synthon for *indole alkaloid synthesis*, is prepared for the first time. The synthesis starts with the condensation of 3-ethyl-4-piperidone **2** with triethyl phosphonoacetate followed by stereoselective hydrogenation of the resulting α,β-unsaturated ester **5** to give 4-piperidineacetate cis-**6** as the major isomer. This was converted in high yield to the target molecule cis-**1** by a two-step sequence through the corresponding β-keto sulfoxide cis-**7**.

We have recently reported the use of 4-acetonylpiperidines as intermediates in the synthesis of more complex polycyclic systems, such as C-7 functionalized 2-azabicyclo[3.3.1]nonanes[2-4] (morphans)[5] and indolo[3,2-f]morphans[2] (6,7-benzomorphan[6] analogues), as well as in the context of our studies directed to the synthesis of Strychnos indole alkaloids.[3,4,7] These acetonylpiperidines were prepared in good yield from 1-methyl- or 1-benzyl-4-piperidone by Wadsworth-Emmons condensation with diethyl 2-oxopropylphosphonate followed by catalytic hydrogenation of the resulting mixture of α,β- and β,γ-unsaturated ketones.

Since several indole alkaloids contain a cis-4-alkyl-3-ethylpiperidine moiety as a portion of the nonaromatic framework (i.e. dasycarpidone, tubifoline), it seemed of interest to apply a similar two-step sequence to obtain cis-4-acetonyl-3-ethylpiperidines.

The required 3-ethyl-4-piperidone **2** was prepared in three steps (52% overall yield) from 1-benzyl-4-piperidone, by methoxycarbonylation, alkylation of the resulting β-keto ester with ethyl iodide in the presence of potassium carbonate and, finally, hydrolysis and decarboxylation with 30% sulfuric acid.[8]

However, condensation of ketone **2** with diethyl 2-oxopropylphosphonate did not

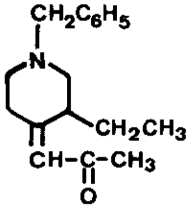


a. Isomer **trans-1** was also obtained in 8% yield

b. Isomer **trans-6** was obtained in 16% yield

Reagents: (i) NaH, C_6H_6, CO_3Me_2; (ii) K_2CO_3, $(CH_3)_2CO$, EtI; (iii) 30% H_2SO_4; (iv) NaH, DME, $(EtO)_2POCH_2COCH_3$; (v) H_2, PtO_2; (vi) NaH, DME, $(EtO)_2POCH_2CO_2Et$; (vii) H_2, Pd-C; (viii) NaH, THF, DMSO; (ix) Zn, EtOH, AcOH.

take place under the reaction conditions we had satisfactorily used[2] in the deethyl series (KOH, EtOH-H_2O, r.t.), probably due to the steric effect of the α-ethyl substituent.[9] Under more drastic conditions (NaH, DME, reflux, 44 h), the reaction occurred, although in low yield (20%), to give a mixture of exocyclic (3) and endocyclic (4) isomeric olefins. Catalytic hydrogenation of this mixture over platinum dioxide afforded a mixture of <u>cis</u>-1 and <u>trans</u>-1 in a nearly equimolecular ratio. After column chromatography, the expected ketone <u>cis</u>-1 was obtained in 8% overall yield from 4-piperidone 2.



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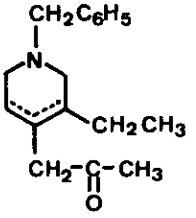
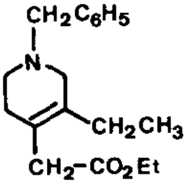


4a: Δ³-isomer

4b: Δ⁴-isomer



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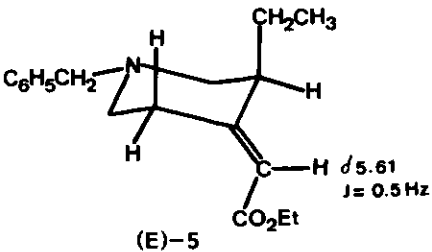
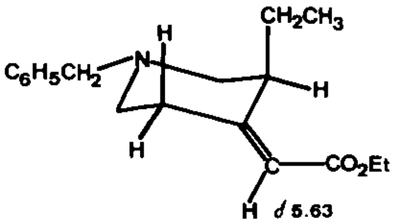
These scarcely satisfactory results prompted us to utilize as condensating agent a phosphonate anion more nucleophilic than the above β-keto phosphonate. In this respect, the conversion of ketone 2 into an epimeric mixture of piperidineacetates **6** in 35% overall yield by means of a Wadsworth-Emmons condensation with triethyl phosphonoacetate followed by hydrogenation had been previously reported.[8a] However, neither the structure of the adduct formed in the condensation step was determined nor separation of the diastereomeric mixture of **6** was effected. Consequently, we decided to reexamine this transformation.[10,11] We focused our interest on the control of Wadsworth-Emmons reaction[12] since, when utilizing 4-piperidones, double bond isomerizations have been observed[13] and the hydrogenation of the resulting exocyclic and endocyclic adducts follows a different stereochemical course. Thus, the hydrogenation of 3-ethylpiperidine-$\Delta^{4,\alpha}$-acetates[10] and related compounds having an exocyclic double bond[14] occurs in high stereoselectivity to give *cis*-3,4-disubstituted piperidines whereas the *trans* isomers are the major products in the hydrogenation of endocyclic isomers.[10a]

We found that the best reaction conditions were the use of a 1:1.08:1.38 ratio of starting ketone **2**, sodium hydride as the base, and phosphonoacetate, respectively, operating at 70°C for 2 h in DME solution. Under these conditions the desired α,β-unsaturated ester **5** was obtained in 88% yield as a 7:3 mixture of *E* and *Z* isomers. In contrast, when an excess of sodium hydride was used (see Experimental), the endocyclic olefin **8** was the only isomer obtained.

The assignment of the *E* double bond configuration to the major isomer of **5** was inferred from the coupling constant of the doublet due to the vinyl proton in the ^{1}H-nmr spectrum (J = 0.5 Hz; compare with J = 1.8 Hz in the minor *Z* isomer), taking into account that transoid allylic coupling constants are smaller than cisoid ones.[15] The multiplicity of these signals clearly indicated that in both cases only one allylic coupling exists,[16] which implies a preferred conformation having the ethyl substituent in a pseudoaxial disposition to avoid the $A^{1,3}$-strain.[17]



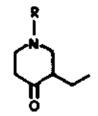
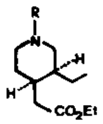
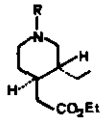
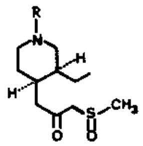
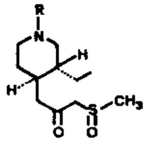
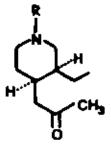
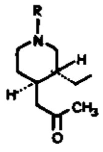
(*E*)-5



(*Z*)-5

As expected, catalytic hydrogenation of the exocyclic olefin **5** furnished an epimeric mixture of *cis*- and *trans*-**6**, enriched in the *cis* isomer (7:2 ratio), which was separated by column chromatography. The conversion of ester *cis*-**6** into

Table 1. ^{13}C-NMR Chemical Shifts[a] of Piperidines (R = $CH_2C_6H_5$)

	 2	 cis-6	 trans-6	 cis-7	 trans-7	 cis-1	 trans-1
CH_2Ar	61.8	63.3	63.4	63.2	63.3	63.3	63.4
2-C	58.4	55.3	58.3	55.3	58.2	55.4	58.3
3-C	51.3	40.1	41.8	40.0	41.5/41.4	40.0	41.8
4-C	210.6	34.8[b]	37.1	33.1[b]	35.5	33.4[b]	35.8
5-C	40.8	28.5	31.6	28.6	31.8	28.5	31.8
6-C	53.5	52.2[b]	53.3	52.1[b]	53.1	52.2[b]	55.2
$\underline{C}H_2CH_3$	20.6	20.0[b]	23.8	20.1[b]	23.9	20.1[b]	23.9
$CH_2\underline{C}H_3$	11.7	12.0	10.9	12.0	10.9	12.0	11.0
4-CH_2	——	35.7[b]	38.6	46.4[b]	49.4/49.3	44.6[b]	47.8
Ar	138.2	138.8	138.4	138.7	138.1	138.9	138.1
	128.7	128.9	129.1	128.9	129.1	128.8	129.2
	128.3	128.1	128.1	128.1	128.1	128.0	128.1
	127.2	126.8	126.9	126.9	126.9	126.7	127.0
Others		$CO_2CH_2CH_3$		$COCH_2SOCH_3$		$COCH_3$	
		172.1	173.3	202.0	202.5	207.7	209.3
		60.1	60.1	64.5/64.2	64.6/64.3	30.4	30.6
		14.3	14.3	39.0	39.0	——	——

[a] In ppm relative to TMS. Measured in $CDCl_3$. [b] Broad signal.

methyl ketone **cis-1** was accomplished in excellent yield by a two-step sequence, through the corresponding α-sulfinyl ketone **cis-7**. Thus, exposure of ester **cis-6** to the ylid of dimethyl sulfoxide[18] in THF gave β-keto sulfoxide **cis-7** in 93% yield. Both ^{1}H- and ^{13}C-nmr spectra indicated that **cis-7** was stereochemically non-homogeneous due to the presence of the new chiral center (sulfur atom) in the molecule. Finally, the reduction of β-keto sulfoxide **cis-7** was effected by treatment with zinc dust in acetic acid solution at 65°C for 12 h.[19]

By a similar two-step sequence, the minor piperidineacetate **trans-6** was elaborated into ketone **trans**-1 in 75% overall yield.

The relative configuration of 3-ethylpiperidines prepared in this work was evident from their ^{1}H-nmr data. In the cis series the spectra are simpler than those of trans isomers as a consequence of the equilibrium between two chair conformations and the most significant signal is the doublet due to the methylene protons attached to the 4-position of the piperidine ring. In contrast, these protons are not equivalent in the trans isomers, in which they appear as an ABX system.[20] On the other hand, in the ^{13}C-nmr spectra of cis isomers, the absorptions due to C-4, C-6, and the methylene carbons attached to C-3 and C-4 appear as broad signals due to the conformational inversion[21] of the piperidine ring.

In conclusion, a convenient (35% overall yield), stereoselective synthesis of cis-4-acetonyl-1-benzyl-3-ethylpiperidine (**cis**-1), a potential synthon for indole alkaloid synthesis, is reported.

EXPERIMENTAL

^{1}H-Nmr spectra were recorded in $CDCl_3$ on a Varian XL-200 spectrometer or, when indicated, in CCl_4 on a Perkin-Elmer R-24B (60 MHz) instrument using TMS as internal standard. ^{13}C-Nmr spectra were determined on a Varian XL-200 spectrometer (50.3 MHz). The chemical shifts are reported in ppm downfield (δ) from TMS. Ir spectra were taken with a Perkin-Elmer 577 spectrophotometer, and only noteworthy absorptions (reciprocal centimeters) are listed. GLC was run isothermally on a Perkin-Elmer F-11 chromatograph fitted with a flame ionization detector. Prior to concentration under reduced pressure, all organic extracts were dried over anhydrous sodium sulfate powder. TLC and column chromatography were carried out on SiO_2 (silica gel 60, Merck 0.063-0.200 mm), and the spots were located with uv light or iodoplatinate reagent. Unless otherwise noted, distillations were effected using a Büchi GKR-50 Kugelrohr apparatus and the temperatures cited are the maximum temperatures of the oven during the distillation. Dimethoxyethane (DME) and tetrahydrofuran (THF) were purified and dried by distillation from $LiAlH_4$. Dimethyl sulfoxide (DMSO) was distilled from CaH_2 at reduced pressure. Previously to use, the suspension of sodium hydride in mineral oil was washed three times with anhydrous benzene or hexane. Microanalyses were performed on a Carlo Erba 1106 analyzer by Instituto de Química Bio-Orgànica, Barcelona.

1-Benzyl-3-ethyl-4-piperidone (2)

Dimethyl carbonate (26.8 ml, 0.32 mol) was added dropwise under nitrogen to a suspension of sodium hydride (55%, 19.8 g, 0.45 mol) in anhydrous benzene (350 ml). After the addition of a few drops of methanol, the mixture was heated at reflux and a solution of 1-benzyl-4-piperidone (30 g, 0.16 mol) in benzene (100 ml) was added dropwise for 35 min. Heating was maintained until the evolution of hydrogen ceased (2.5 h). The reaction mixture was cooled, stirred at room temperature for 2 h, and acidified by careful addition of glacial acetic acid. The resulting mixture was diluted with ice-cold water and adjusted to pH 8 with aqueous ammonium hydroxide. The benzene layer was separated and the aqueous phase was extracted with benzene. The combined benzene solutions were dried and evaporated to afford crude **ethyl 1-benzyl-4-oxo-3-piperidinecarboxylate** (38.4 g): ir (NaCl) 1735 (CO ester), 1710 (CO ketone), 1650 (enol ester), 1610 (C=C enol); nmr (60 MHz) 2.3–2.8 (m, 4H, 5- and 6-CH_2), 3.0 (s, 2H, 2-CH_2), 3.5 (s, 2H, CH_2Ar), 3.6 (s, 3H, OCH_3), 7.1 (s, 5H, ArH).

To a suspension of anhydrous potassium carbonate (80.1 g, 0.58 mol) and the above ß-keto ester (36 g, 0.15 mol) in anhydrous acetone (250 ml) was added under nitrogen a solution of ethyl iodide (23.7 ml, 0.29 mol) in anhydrous acetone (250 ml). The mixture was refluxed for 6 h until the ferric chloride test was negative. The inorganic materials were filtered and washed with acetone. The evaporation of the combined filtrates gave an oily residue, which was dissolved in methylene chloride and washed with water. Evaporation of dried organic extract left crude **ethyl 1-benzyl-3-ethyl-4-oxo-3-piperidinecarboxylate** (35.8 g): ir (NaCl) 1710–1740 (CO); nmr (60 MHz) 0.80 (t, 3H, CH_3), 1.4–3.2 (m, 8H), 3.5 (s, 2H, CH_2Ar), 3.6 (s, 3H, OCH_3), 7.1 (s, 5H, ArH).

Aqueous 30% H_2SO_4 (400 ml) was slowly added under nitrogen to the above alkylated ß-keto ester (24 g, 0.087 mol). The mixture was refluxed for 6 h with vigorous stirring, cooled, basified with cold concentrated aqueous sodium hydroxide solution, and extracted with methylene chloride. Evaporation of the solvent from the extracts left a crude material, which was distilled to give piperidone **2** (10.94 g, 52% overall yield from 1-benzyl-4-piperidone): bp 99-101°C/0.25 mmHg [Lit.[8a] 138-139°C/1 mmHg]; ir (NaCl) 1700 (CO); nmr 0.87 (t, 3H, CH_3), 1.29–1.33 (m, 1H), 1.79–1.83 (m, 1H), 2.24–2.52 (m, 5H), 2.96–3.06 (m, 2H), 3.55 and 3.67 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 7.34–7.37 (m, 5H, ArH). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.37; H, 8.81; N, 6.44. Found: C, 77.39; H, 8.75; N, 6.57.

Condensation of Ketone 2 with Diethyl 2-Oxopropylphosphonate Followed by Catalytic Hydrogenation

To a suspension of sodium hydride (55%, 1.2 g, 27 mmol) in DME (10 ml) was added a solution of diethyl 2-oxopropylphosphonate[22] (5.35 g, 27 mmol) in DME (5 ml). After stirring for 10 min, a solution of ketone **2** (2 g, 9 mmol) in DME (5 ml) was added under nitrogen, and the mixture was refluxed for 44 h. The solvent was evaporated and the residue was partitioned between methylene chloride and 1.5 N hydrochloric acid. The organic layer was discarded and the aqueous phase was basified with 2 N aqueous sodium hydroxide and extracted with ether. Evaporation of the dried ethereal extract gave a mixture of the starting piperidone **2** and ketones **3** and **4**, which, without further purification, was dissolved in ethanol (15 ml) and hydrogenated at room temperature and atmospheric pressure over platinum dioxide (100 mg). The catalyst was filtered off and the filtrate was concentrated to give an oil, which was chromatographed. Elution with 1:1 benzene-chloroform gave ketone **cis**-1 (185 mg, 8%; see below for spectroscopic and analytical data). Elution with chloroform gave ketone **trans**-1 (175 mg, 8%; see below for spectroscopic data). In some runs, **4-acetonyl-1-benzyl-3-ethyl-1,2,5,6-tetrahydropyridine** (**4a**) was obtained on elution with benzene-chloroform (3:7): nmr 0.95 (t, 3H, CH_3), 1.99 (q, 2H, $C\underline{H}_2CH_3$), 2.16 (s, 3H, $COCH_3$), 2.2 (masked, 2H, 5-CH_2), 2.67 (t, $\underline{J}$ = 6 Hz, 2H, 6-CH_2), 3.07 (s, 2H, 2-CH_2), 3.16 (s, 2H, CH_2CO), 3.73 (s, 2H, CH_2Ar), 7.31-7.41 (m, 5H, ArH).

Ethyl 1-Benzyl-3-ethylpiperidine-$\Delta^{4,\alpha}$-acetate (5)

Triethyl phosphonoacetate (4.25 ml, 21.3 mmol) was added dropwise under nitrogen to a suspension of sodium hydride (55%, 720 mg, 16.6 mmol) in DME (15 ml) maintained at room temperature. After the addition was complete, the clear solution was stirred for an additional 10-min period. Then, a solution of ketone **2** (3.34 g, 15.4 mmol) in DME (10 ml) was added. The reaction mixture was warmed at 70°C for 2 h. The solvent was evaporated and the residue was partitioned between ether and 1.5 N hydrochloric acid. The ethereal solution was discarded and the aqueous layer was basified with 2 N aqueous sodium hydroxide and extracted with ether. Evaporation of the dried extract gave the α,β-unsaturated ester **5** (3.9 g, 88%) as a 7:3 mixture of $\underline{E}$ and $\underline{Z}$ isomers (determined by GLC): bp 170°C/0.3 mmHg; ir (NaCl) 1710 (CO), 1650 (C=C); nmr 0.82 and 0.84 (2t, 3H, CH_3), 1.25 and 1.26 (2t, 3H, $OCH_2C\underline{H}_3$), 3.38 and 3.55 (2d, $\underline{J}$ = 13 Hz, 1H each, CH_2Ar), 4.12 and 4.13 (2q, 2H, OCH_2), 5.61 (d, $\underline{J}$ = 0.5 Hz, 0.7H, =CH, $\underline{E}$-isomer), 5.63 (d, $\underline{J}$ = 1.8 Hz, 0.3H, =CH, $\underline{Z}$-isomer), 7.29-7.32 (m, 5H, ArH). Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.23; H, 8.76; N, 4.87. Found: C, 75.10; H, 8.93; N, 4.70.

Ethyl 1-Benzyl-3-ethyl-1,2,5,6-tetrahydro-4-pyridineacetate (8)

Operating as above, from sodium hydride (55%, 600 mg, 13.8 mmol), DME (25 ml), triethyl phosphonoacetate (2.28 ml, 11.5 mmol), and ketone **2** (2 g, 9.2 mmol), after warming at 70°C for 5 h, the β,γ-unsaturated ester **8** (1.54 g, 58%) was obtained as the sole product. An analytical sample was obtained by Kugelrohr distillation: bp 170°C/0.3 mmHg; ir (NaCl) 1735 (CO); nmr 0.94 (t, $\underline{J}$ = 7.5 Hz, 3H, CH_3), 1.22 (t, 3H, $OCH_2C\underline{H}_3$), 1.99 (q, 2H, $C\underline{H}_2CH_3$), 2.15 (br s, 2H, 5-CH_2), 2.52 (t, $\underline{J}$ = 6 Hz, 2H, 6-CH_2), 2.92 (br s, 2H, 2-CH_2), 3.01 (s, 2H, CH_2CO), 3.56 (s, 2H, CH_2Ar), 4.09 (q, 2H, OCH_2), 7.24-7.32 (m, 5H, ArH). Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.23; H, 8.76; N, 4.87. Found: C, 75.21; H, 8.98; N, 4.95.

Ethyl 1-Benzyl-3-ethyl-4-piperidineacetate (6)

Unsaturated ester 5 (10.2 g, 35 mmol) was dissolved in ethanol (70 ml) and hydrogenated at room temperature and atmospheric pressure over 10% palladium on charcoal (1.02 g). When the solution had absorbed the required volume of hydrogen, the catalyst was filtered off and the filtrate was concentrated to leave an oil, which was chromatographed. Elution with hexane-ethyl acetate (4:1) gave ester ***cis*-6** (5.5 g, 55%); bp 71-73°C/0.03 mmHg (distillation carried out on a Fischer spaltrohr MMS 152 microcolumn); [Lit.[8a] 142-145°C/0.3 mmHg]; ir (NaCl) 1735 (CO); nmr 0.80 (t, 3H, CH_3), 1.24 (t, 3H, $OCH_2\underline{CH_3}$), 2.26 (d, *J* = 7 Hz, 2H, CH_2CO), 3.28 and 3.54 (2d, *J* = 13.2 Hz, 1H each, CH_2Ar), 4.12 (q, 2H, $OC\underline{H_2}CH_3$), 7.30 (m, 5H, ArH). Elution with hexane-ethyl acetate (7:3) gave ester ***trans*-6** (1.59 g, 16%); ir (NaCl) 1735 (CO); nmr 0.83 (t, 3H, CH_3), 1.24 (t, 3H, $OCH_2\underline{CH_3}$), 1.92 (td, *J* = 12, 12, and 2.4 Hz, 1H, $6\text{-}H_{ax}$), 2.03 (dd, *J* = 14.5 and 8.8 Hz, 1H, CH_2CO), 2.56 (dd, *J* = 14.5 and 4 Hz, 1H, CH_2CO), 2.80 (dd, *J* = 12 and 3 Hz, 1H, $2\text{-}H_{eq}$), 2.92 (ddd, *J* = 12, 4, and 2 Hz, 1H, $6\text{-}H_{eq}$), 3.43 and 3.56 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 4.12 (q, 2H, OCH_2), 7.30 (m, 5H, ArH).

When the volume of hydrogen was not controlled, the reduction was accompanied with hydrogenolysis of the benzyl group. This process was not observed when platinum dioxide was used as catalyst.

cis-4-Acetonyl-3-ethylpiperidine (*cis*-1)

Sodium methylsulfinylmethanide was prepared according to the procedure reported by Corey,[18] from sodium hydride (55%, 1.56 g, 36 mmol), DMSO (22 ml, 0.31 mol), and THF (57 ml). To this solution was added dropwise at 0-5°C a solution of ester ***cis*-6** (3.35 g, 11.6 mmol) in THF (10 ml). After being stirred at room temperature for an additional 3-h period, the mixture was poured into ice-water (100 ml), adjusted to pH 8 with 1.2 N hydrochloric acid, and extracted with methylene chloride. The extract was washed with brine and dried. Evaporation of the solvent gave **1-(*cis*-1-benzyl-3-ethyl-4-piperidyl)-3-(methylsulfinyl)-2-propanone** (***cis*-7**, 3.58 g, 93%) which was directly used in the next reaction; ir (NaCl) 1710 (CO), 1025 (S=O); nmr 0.79 (t, 3H, CH_3), 2.56 (d, *J* = 6.5 Hz, 2H, CH_2CO), 2.67 (s, 3H, $SOCH_3$), 3.43 and 3.53 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 3.67, 3.70, 3.80, and 3.82 (4d, *J* = 13.6 Hz, 0.5H each, $COCH_2SO$), 7.30 (m, 5H, ArH).

A solution of sulfoxide ***cis*-7** (3.9 g, 12.1 mmol) in absolute ethanol (6.7 ml) and glacial acetic acid (3.5 ml) was added dropwise to a vigorously stirred mixture of zinc dust (3.96 g, 0.06 g-atom), absolute ethanol (6.7 ml), and glacial acetic acid (3.5 ml). The resulting mixture was warmed at 65°C for 12 h. The suspended solids were removed by filtration and washed by slurrying in benzene and filtering. The solution was diluted with water (25 ml), neutralized by careful addition of powdered sodium carbonate, and decanted. The aqueous phase was extracted with ether. The combined organic extracts were washed with aqueous sodium bicarbonate, dried, and evaporated to give ketone

cis-1 (2.6 g, 85%). An analytical sample was obtained by Kugelrohr distillation: bp 180-190°C/ 0.7 mmHg; ir (NaCl) 1710 (CO); nmr 0.80 (t, 3H, CH_3), 1.1-1.6 (m, 5H), 2.1-2.7 (m, 5H), 2.14 (s, 3H, $COCH_3$), 2.38 (d, *J* = 7 Hz, 2H, CH_2CO), 3.46 and 3.64 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 7.27-7.36 (m, 5H, ArH). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.73; H, 9.70; N, 5.39. Found: C, 79.00; H, 9.93; N, 5.39.

trans-4-Acetonyl-1-benzyl-3-ethylpiperidine (trans-1)

Operating as above, ester **trans-6** (950 mg, 3.30 mmol) was converted to β-keto sulfoxide **trans-7** (980 mg, 89%): nmr 0.82 (t, 3H, CH_3), 1.97 (td, *J* = 12, 11.5, and 3 Hz, 1H, 6-H_{ax}), 2.3-2.8 (m, 2H, CH_2CO), 2.94 (ddd, *J* = 11.5, 4, and 2 Hz, 1H, 6-H_{eq}), 3.42 and 3.55 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 3.70 and 3.71 (2d, *J* = 13.5 Hz, 0.5H each, $COCH_2SO$), 3.80 (d, *J* = 13.5 Hz, 1H, $COCH_2SO$), 7.30 (m, 5H, ArH). This sulfoxide (890 mg, 2.76 mmol) was reduced, as in the above *cis* series, with zinc dust (900 mg, 0.013 g-atom) in ethanol (6 ml) and glacial acetic acid (3 ml) to give ketone **trans**-1 (610 mg, 85%); ir (NaCl) 1710 (CO); nmr 0.82 (t, 3H, CH_3), 1.04-1.72 (m, 6H), 1.80 (dd, *J* = 11 and 11 Hz, 1H, 2-H_{ax}), 2.02 (td, *J* = 11, 11, and 2.5 Hz, 1H, 6-H_{ax}), 2.13 (s, 3H, $COCH_3$), 2.19 (dd, *J* = 16.5 and 8.5 Hz, 1H, CH_2CO), 2.65 (dd, *J* = 16.5 and 3.5 Hz, 1H, CH_2CO), 2.86 (dd, *J* = 11 and 3 Hz, 1H, 2-H_{eq}), 2.99 (td, *J* = 11, 4, and 2 Hz, 1H, 6-H_{eq}), 3.51 and 3.63 (2d, *J* = 13 Hz, 1H each, CH_2Ar), 7.24-7.37 (m, 5H, ArH).

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