Structure, Stereochemistry, and Conformation of Diastereoisomeric *cis*- and *trans*-3-Ethyl-1,2,3,4,4a,9a-Hexahydrocarbazol-4-ones by Means of ^{13}C and Two-dimensional ^{1}H Nuclear Magnetic Resonance Spectroscopy. An Example of Diastereoselection in a Photocyclisation Reaction[1]

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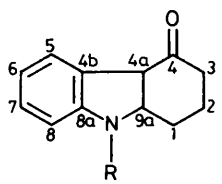
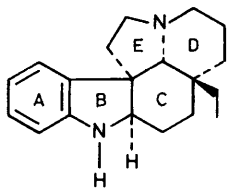
3-Ethyl hexahydrocarbazol-4-ones (**3a**) and (**3b**) are stereospecifically obtained in a 4a,9a-*trans*-stereochemistry by a photocyclisation reaction in which appreciable diastereoselection (40%) due to the ethyl chain is observed. They are quantitatively converted into *cis*-compounds by treatment with acid or by angular alkylation *via* a benzylic carbanion. Complete analysis of the ^{1}H (1D, 2D) NMR spectra allows the conformation of the c ring in each compound to be established. Moreover, the collected ^{1}H and ^{13}C NMR data constitute references for further identification of the *cis*- and *trans*-series and further determination of the position of the 3-ethyl chain. Equilibrium studies between the different isomers show the higher stability of the *cis*-derivatives which possess the stereochemistry of the natural products of the *Aspidosperma* indole alkaloids.

The tricyclic system of hexahydrocarbazoles constitutes a part of the *Aspidosperma* alkaloid skeleton. The corresponding hexahydrocarbazol-4-ones, with a keto group which permits the building of the two complementary rings, can be used as key intermediates in the synthesis of *Aspidosperma* derivatives,[2] characterised by interesting biological activity.[3] They can be prepared by non-oxidative photocyclisation of tertiary aryl enaminones[4] in agreement with the reactions studied by Grellmann[5] and Chapman[6] from diphenylamines and arylenamines.

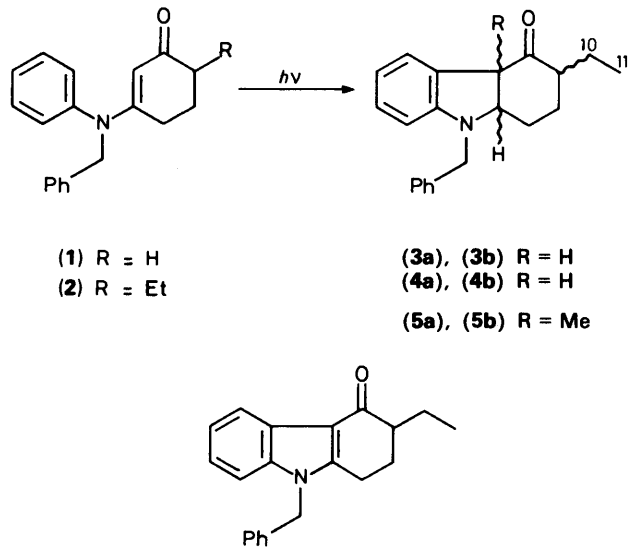




Aspidospermidine

One of the strategies involves the introduction of the C(3) ethyl chain, present in most of these alkaloids, at the first step of the synthesis *i.e.* on the enaminone (**1**).[7] Thus, 3-ethylhexahydrocarbazolone was generated from (**2**), in two diastereoisomeric forms (**3a**, **b**) [ratio 30:70 (84% yield)] (Scheme 1). Referring to previous results,[4] a *trans*-4a,9a-stereochemistry can be expected for these derivatives; however the presence of the ethyl group and of two epimerisable centres may complicate or modify the situation.

The behaviour of derivatives (**3a**, **b**) was studied in acidic and basic conditions. Acidic treatment (stirring on silica gel or refluxing in CH_2Cl_2 in the presence of a catalytic amount of camphorsulphonic acid) transformed the mixture of (**3a**) + (**3b**) into two other diastereoisomers (**4a**, **b**) in approximately the same ratio. The reaction, realised on pure compounds, afforded (**4a**) from (**3a**) and (**4b**) from (**3b**); stronger acidic conditions were found to destroy the molecule. On the other hand, in smooth basic conditions (elution through an alumina column), compounds (**3a**, **b**) were unstable, being oxidised to the tetrahydro derivative (**6**).



(**1**) R = H
(**2**) R = Et

(**3a**), (**3b**) R = H
(**4a**), (**4b**) R = H

(**5a**), (**5b**) R = Me

(**6**)

Scheme 1.

The introduction of a substituent, by alkylation at C(4a), should prevent this oxidation and constitute the starting point of the E ring. Thus, methylation of (**3a**) + (**3b**) with CH_3I (KH, THF) generated (**5a**) + (**5b**) [ratio 30:70 (84% yield)]. The equilibration in acidic medium of pure (**5a**) or pure (**5b**) afforded a mixture of (**5a**) + (**5b**) in equal amounts.

The hexahydrocarbazolones (**3a**, **b**), (**4a**, **b**), and (**5a**, **b**) belong to a new series with three asymmetric centres. The determination of their stereochemistry and relative stability is essential before they can be involved in a synthetic scheme for pentacyclic alkaloids. The present work uses ^{1}H (1D, 2D) and ^{13}C NMR data to establish the stereochemistry and the conformation of the molecules and to study the equilibrium between the different isomers. Moreover, these data constitute a very useful source of spectroscopic references for the assignment of the stereochemistry of further synthetic intermediates and the conform

Table 1. ^{1}H NMR chemical shifts [δ(ppm)] of compounds (**3a, b**), (**4a, b**), and (**5a, b**) in $CDCl_3$.

Proton	Splitting pattern	(3a)	(3b)	(4a)	(4b)	(5a)	(5b)
Me(11)	t	1.00	1.00	0.94	0.91	0.80	0.84
H(10B)[a]	ddq	1.33	1.62	1.40	1.30	1.25	1.18
Me(4a)	s	—	—	—	—	1.35	1.48
H(10A)[a]	ddq	1.95	1.86	1.86	1.84	1.74	1.76
$H(2)_{ax}$	dddd	1.38	1.87	1.34	1.79	1.23	1.70
$H(1)_{ax}$	dddd	1.90	2.01	1.72	1.90	1.68	1.87
$H(1)_{eq}$	dddd	2.20	2.01	2.00	2.13	1.80	2.08
$H(2)_{eq}$	dddd	2.26	1.95	2.02	1.92	2.00	1.82
H(3)	dddd	2.36	2.39	2.28	2.21	2.32	2.27
H(9a)	ddd	3.12	3.15	4.07	4.10	—	—
H(9a)	dd	—	—	—	—	3.61	3.62
H(4a)	d	3.72	3.81	3.96	3.77	—	—
NCH_2Ph	s	4.27	4.27	—	—	—	—
NCH_2Ph	AB system	—	—	4.36	4.31	4.32	4.26
H(8)	d	6.56	6.56	6.50	6.46	6.40	6.40
H(6)	dd	6.86	6.86	6.74	6.76	6.60	6.75
H(7)	dd	7.12	7.12	7.11	7.09	7.01	7.05
H(5)	d	7.52	7.37	7.07	7.26	6.90	7.16
Ph	m	7.58	7.58	7.39	7.36	7.30	7.30

[a] The codings A and B refer to the proton at lower- and higher-field sites respectively.

Table 2. Determination of dihedral angles from the apparent ^{1}H–^{1}H coupling constants.

Compound	Proton pair	^3J/Hz	θ_{CH-CH}[a]/°	Compound	Proton pair	^3J/Hz	θ_{CH-CH}[a]/°
(3a)	9a, 4a	14.0	−160	(3b)	9a, 4a	15.0	−165
	9a, 1_{ax}	11.5	+170				
	9a, 1_{eq}	2.5	−70		9a, 1_{ax} / 9a, 1_{eq}	14.5	*b*
	3, 2_{ax}	12.0	−150				
	3, 2_{eq}	6.0	−30				
	2_{ax}, 1_{ax}	12.0	+165		3, 2_{ax} / 3, 2_{eq}	7.5	*c*
	2_{ax}, 1_{eq}	4.0	+45				
(4a)	9a, 4a	9.0	+10	(4b)	9a, 4a	8.5	−10
	9a, 1_{ax}	8.5	−165		9a, 1_{ax}	3.0	+60
	9a, 1_{eq}	5.0	−45		9a, 1_{eq}	3.0	−60
	3, 2_{ax}	10.0	−160		9a, 2_{eq}	1.5	
	3, 2_{eq}	6.0	−40		3, 2_{ax}	12.0	+160
					3, 2_{eq}	6.0	+40
					2_{ax}, 1_{ax}	13.5	−180
					2_{ax}, 1_{eq}	3.0	−60
(5a)	9a, 1_{ax}	8.0	−160	(5b)	9a, 1_{ax}	3.0	+60
	9a, 1_{eq}	5.0	−40		9a, 1_{eq}	3.0	−60
	3, 2_{ax}	10.0	−160		9a, 2_{eq}	1.0	
	3, 2_{eq}	6.0	−40		3, 2_{ax}	11.0	+160
					3, 2_{eq}	6.0	+40
					2_{ax}, 1_{ax}	13.0	−180
					2_{ax}, 1_{eq}	3.0	−60

[a] Positive angles are measured clockwise and negative angles anticlockwise. [b] H(9a) essentially axial. [c] H(3) essentially equatorial.

ation of the relatively flexible C ring which may adopt various forms of very similar energy.

Results

Analysis of Spectra: Stereochemical and Conformational Results.—*(a)* ^{1}*H(1D, 2D) NMR spectroscopy.* As a starting point, the ^{1}H (1D) spectra of compounds (**3a, b**), (**4a, b**), and (**5a, b**) were recorded (Table 1). The stereochemistry of the different isomers was established from the coupling constants of H(9a) and H(3) with their vicinal hydrogens in the C-ring *via* the corresponding dihedral angle values (Table 2), these latter deduced approximately from the Karplus equation[8] or from the Williamson–Johnson equation adapted for cyclohexanones.[9] This determination of angles is not absolutely rigorous because of the influence of factors other than geometrical ones, but allows, at least, the assignment of an 'essentially axial' or 'essentially equatorial' situation to the corresponding protons.[10] In particular $^3J_{9a,4a}$ allows the determination of the *cis* or *trans* relationship between the two hydrogens, and $^3J_{3,2}$ allows the stereochemistry of the side chain to be deduced.

However, protons H(1), H(2), and H(3), each one coupled with four hydrogens, were difficult to identify. In order to locate them, COSY ^{1}H–^{1}H chemical shift correlations were performed on isomers (**3a**), (**3b**), (**4a**), and (**4b**). Thus, from the signals of

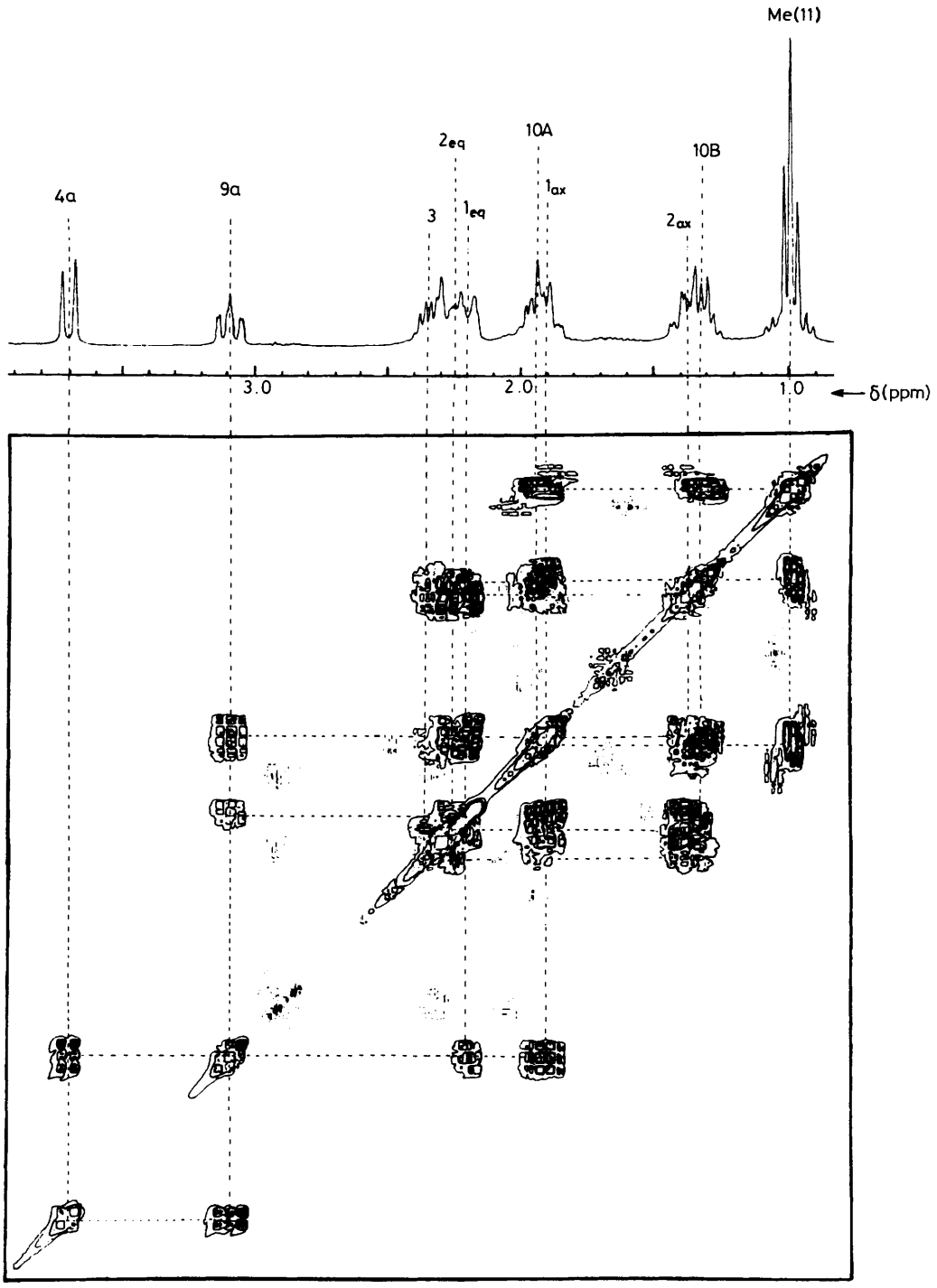


Figure. 300 MHz COSY spectrum of (**3a**) in $CDCl_3$ at 298 K presented as a contour plot (δ 0.8 to 3.9 ppm).

H(4a) (d, δ *ca.* 3.8–3.9 ppm) and Me(11) (t, δ *ca.* 0.95–1.0 ppm) the following sequence could be assigned by this experiment: H(4a)–H(9a)–$H(1)_{ax}$–$H(1)_{eq}$–$H(2)_{ax}$–$H(2)_{eq}$–H(3)–H(10A)–H(10B)–Me(11) (Figure, COSY spectrum of (**3a**) as example).

The absolute values of J_{gem} for the C ring methylenes were found to be approximately 12–13 Hz. They could be measured on the signals of hydrogens $H(2)_{ax}$ for compounds (**3a**) and (**4a**), and $H(1)_{ax}$ and $H(1)_{eq}$ for compound (**4a**). The splittings of H(3) due to coupling with the methylene protons in C(10) could be treated, in each compound, as a first-order spectrum (*i.e.* AMX), since the smallest chemical-shift difference observed between H(10A) and H(10B) was 0.24 ppm (*i.e.* 72 Hz at 300 MHz), $J_{10A,10B}$ being equal to 14 Hz. In contrast, the splittings of H(3) due to coupling with the two H(2) atoms as well as the splittings of H(9a) due to coupling with the two H(1) atoms had to be considered either as an AMX or an ABX system depending on the compound.

Compounds (**3a**) *and* (**3b**). A *trans*-configuration of the B/C ring junction can be assigned from the high values of $^3J_{4a,9a}$ [14 Hz in (**3a**), 15 Hz in (**3b**)], corresponding to two axial hydrogens with a dihedral angle of approximately 160–165°.

Moreover, in compound (**3a**), the sequence H(9a)–$H(1)_{ax}$–$H(2)_{ax}$–H(3) with large coupling constants (J = 11.5–12 Hz) is characteristic of a chair conformation with axial H(9a) and H(3)

Table 3. ^{13}C NMR chemical shifts [δ(ppm)] of compounds (**3a, b**) and (**5a, b**) in $CDCl_3$.

Compound	C=O	C(6)	C(8)	C(3)	C(8a)	Me(11)
trans (**3a**)	206.2	119.4	108.9	51.7	153.1	11.9
trans (**3b**)	208.8	119.4	108.9	51.4	152.9	12.0
cis (**4a**)	210.9	118.2	107.6	48.8	150.9	11.4
cis (**4b**)	210.7	118.3	107.9	51.1	152.4	11.7
cis (**5a**)	212.4	118.1	107.4	46.9	150.4	11.4
cis (**5b**)	213.9	118.3	107.8	49.3	151.8	11.7

protons, an equatorial ethyl group and the following dihedral angles: H–C(9a)–C(1)–H_{ax} *ca.* 170°, H–C(3)–C(2)–H_{ax} *ca.* 150° and H_{ax}–C(2)–C(1)–H_{ax} *ca.* 165°.

In compound (**3b**), the small chemical shift difference between $H(1)_{ax}$ and $H(1)_{eq}$ ($\Delta\delta < 0.08$ ppm = 24 Hz) (Table 1) suggests the consideration of the splittings attributed to the H(9)–2H(1) and H(3)–2H(2) interactions as two ABX systems with 'invisible' AB parts, hidden within the methylene envelope. However the $J_{AX,BX}$ values [14.5 Hz for H(9a) and 7.5 Hz for H(3)] confirm the 'essentially axial' character of H(9a) and indicate the 'essentially equatorial' character of H(3). However the difficulty of measuring complementary coupling constants in the spectrum prevents the determination of the exact C ring conformation. This latter may be either a chair form with an axial ethyl group [as shown by the $J_{AX} + J_{BX}$ value of H(3)] or a twisted form with a quasi-equatorial ethyl group, or, indeed, any intermediate form. On the basis of energetic considerations, the difference in free energy between the two axial and equatorial positions of an 2-ethyl group on a chair form of a cyclohexanone ring[11] was found to be only 4.6 kJ mol^{-1}, while the energy difference between the chair and twisted forms of a cyclohexanone was estimated[12] to be 11.3 kJ mol^{-1}. Those values were established in a monocyclic system; they may be slightly, but not considerably, modified in a tricyclic one. Their comparison is more favourable to the first hypothesis for (**3b**) *i.e.* a pseudo-chair form with an axial ethyl group. This result is also in agreement with the NMR data mentioned above.

Consequently, compounds (**3a, b**) have both a *trans*-junction with two *trans*-axial hydrogens H(4a) and H(9a) and two bonds of the dihydroindolic ring in a favourable quasi-equatorial position. The C ring is deduced to be approaching a chair with an α-equatorial ethyl group in (**3a**) and a β-axial ethyl group in (**3b**) referring to the α-position of H(9a) in aspidospermidine (Scheme 2).

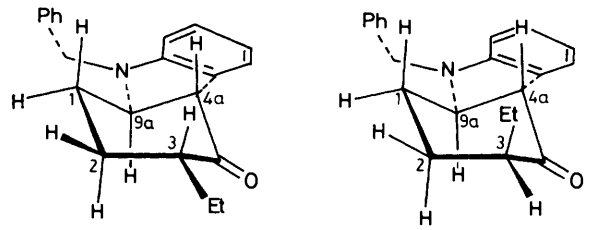
The slight deformation of the C ring compared with a perfect chair is due, as expected, to the presence of the trigonal carbonyl carbon and to the strain created by the fused five-membered ring.

Compounds (**4a**) *and* (**4b**). The *cis*-stereochemistry of the B/C ring junction can be deduced from the intermediate values of $^3J_{4a,9a}$ [9.0 Hz for (**4a**); 8.5 Hz for (**4b**)] corresponding to an axial–equatorial coupling. Moreover, in compound (**4a**), the coupling constants of H(9a) with the two H(1) atoms (8.5 and 5.0 Hz; dihedral angles 165 and 45°) and of H(3) with the two H(2) (10.0 and 6.0 Hz; dihedral angles 160 and 40°) both seem to correspond to 'essentially axial' positions of H(9a) and H(3). However the small value of $^3J_{9a,1_{ax}}$ found for a *trans*-diaxial coupling indicates a deformation of the C ring, compatible with a more flattened chair form.[13]

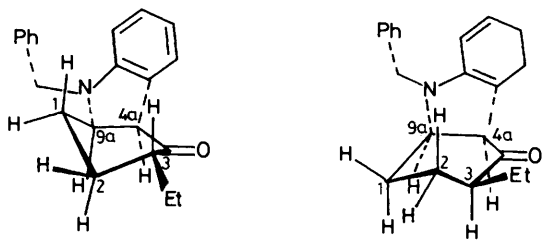
In compound (**4b**), no notable change occurs for H(3) whereas H(9a) now bisects the angle between $H(1)_{ax}$ and $H(1)_{eq}$ ($^3J_{9a,1_{ax}} = {}^3J_{9a,1_{eq}} = 3$ Hz) and occupies an 'essentially equatorial' position.

These results suggest that compounds (**4a, b**) correspond to the two chair forms of the C ring as observed in hydrindanone systems.[14,15] In (**4a**), the C(4a)–C(4b) bond is quasi-axial and the C(9)–N bond is quasi-equatorial while in (**4b**), the reverse situation is observed. By flipping the chair, all the axial substituents become equatorial and *vice-versa*. The ethyl group, by virtue of the opposite C(3) configuration of the two isomers, adopts the favourable quasi-equatorial position in each. Consequently, the *cis*-compounds (**4a**) and (**4b**) correspond to the two forms of a flattened chair with both a quasi-equatorial 3-ethyl group either in an α-position [isomer (**4a**)] or in a β-position [isomer (**4b**)] (Scheme 2).

Compounds (**5a**) *and* (**5b**). *cis*-Stereochemistry can be expected for these compounds because of the method of synthesis.[16] This result is now confirmed not by the $^3J_{9a,4a}$ value, since the 4a position is now substituted, but by the form of the NCH_2Ph signal (AB spectrum) and by the chemical shift of H(5) (*ca.* 6.8 ppm). These data are characteristic of a *cis*-B/C ring junction as indicated below. Furthermore the α- and β-positions of the 3-ethyl chain can be respectively attributed to (**5a**) and (**5b**) by comparison of the coupling constants $^3J_{9a,1}$ and $^3J_{3,2}$ with those of (**4a**) and (**4b**). Therefore, compounds (**5a, b**) have the same stereochemistry and conformation as (**4a, b**), respectively.



(**3a**) (**3b**)



(**4a**) R = H (**4b**) R = H
(**5a**) R = Me (**5b**) R = Me

Scheme 2. Representation of compounds (**3a, b**), (**4a, b**), and (**5a, b**) in the aspidospermidine absolute configuration [H(9a) in an α-position].

(b) ^{13}C *NMR Spectroscopy.* The ^{13}C spectra of all compounds are almost identical except for the carbonyl carbon signals which appears at a higher field, and the C(6) and C(8) nuclei which resonate at lower field in the *trans*-derivatives than in the *cis*-ones. Moreover in the *cis*-derivatives, the carbons C(3), C(8a), and Me(11) resonate at higher fields in compounds (**4a**) and (**5a**), which possess an α-ethyl group, than in compounds (**4b**) and (**5b**) which possess a β-ethyl group ($\Delta\delta$ *ca.* 2 ppm).

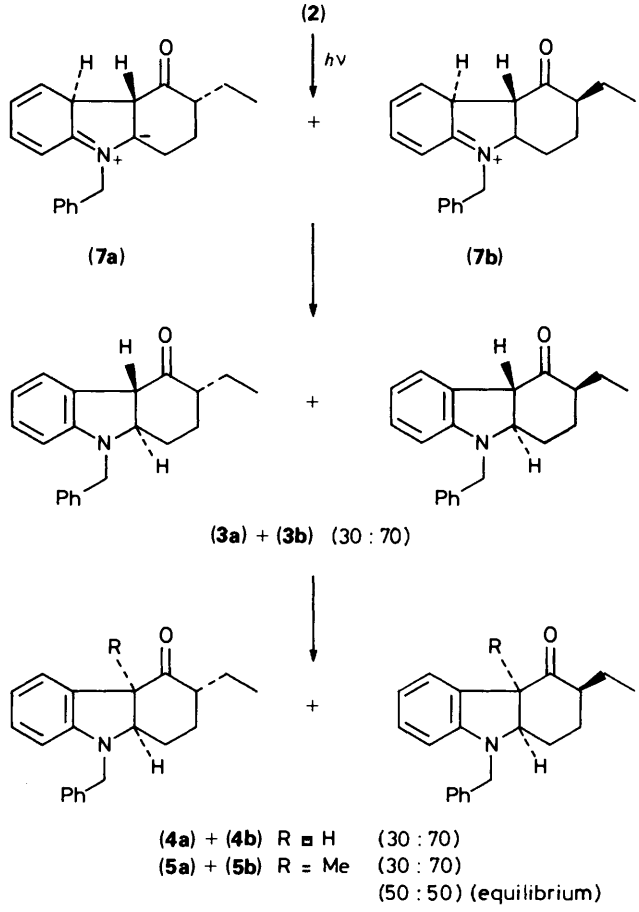
(*c*) *Identification of* cis- *and* trans- *series.* In addition to the coupling constant $^3J_{9a,4a}$ when it exists, several features, deduced from the above results, can be invaluable in distinguishing the *cis*- and *trans*- series: *i.e.* (*i*) in the ^1H NMR spectra, the methylene of NCH_2Ph appears as a singlet in the *trans*- derivatives and as an AB system in the *cis*- ones although the protons are non-equivalent in both cases. Furthermore, in the *trans*-isomers, H(5) is shielded by 0.11–0.45 ppm as previously observed,[16] while H(9a) is strongly deshielded

($\Delta\delta$ = 0.95 ppm); (*ii*) in the ^{13}C NMR spectra, carbons C(6) and C(8) appear at lower field and the carbonyl carbon at higher field in the *trans*-forms. This observation relative to the carbonyl group can be considered as a general rule since it has already been noticed for three pairs of hexahydrocarbazolones;[16] (*iii*) in the IR spectra, the absorption maximum occurs at higher frequency in the *trans*-isomers (ν_{CO} = 1720 cm^{-1}) than in the *cis* (ν_{CO} = 1 700 cm^{-1}), probably because of the higher rigidity and strain of the *trans*-form.

(*d*) *Identification of* cis-α-*ethyl and* cis-β-*ethyl compounds.* The stereochemistry of the 3-ethyl chain in the *cis*-series can be assigned from several data. Thus in ^1H NMR, $^3J_{9a,1_{ax}}$ and $^3J_{9a,1_{eq}}$ are identical in *cis*-β-ethyl compounds (*ca.* 3 or 4 Hz) and different in *cis*-α-ethyl compounds (*ca.* 9 and 6 Hz respectively); in ^{13}C NMR, carbons C(3), C(8), Me(11) appear at higher field in α-ethyl than in β-ethyl compounds.

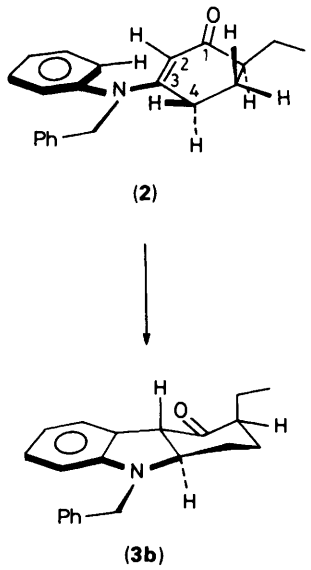
Discussion

From the above results, it is clear that the photocyclisation of the aryl enaminone (**2**) affords, quantitatively and stereospecifically, hexahydrocarbazolones (**3a**, **b**) with a *trans*-relationship at the B/C ring junction, as already observed with their 3-de-ethyl analogues.[4] The reaction involves an helical transition state which cyclises in *trans*-hexahydrocarbazolones *via* two diastereoisomeric zwitterions (**7a**, **b**), generated by a conrotatory reaction[17] (Scheme 3).



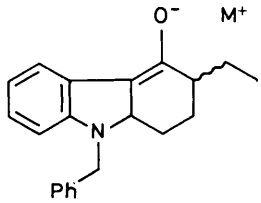
Scheme 3.

The ratio of the two isomers [(**3a**):(**3b**), 30:70] suggests that the ethyl group introduces diastereoselection during the cyclisation. The helical form (**2**), in which the aromatic ring approaches the cyclohexanone from the opposite side of the ethyl chain, seems strongly favoured (Scheme 4). Such an important effect (40% diastereoselection) is remarkable if one considers the large distance between the ethyl group and the first-created asymmetric centre C(4a). In fact, the ethyl chain forces the cyclohexanone ring into a half-chair conformation, in which the hydrogens on C(4) are, respectively, quasi-axial and quasi-equatorial (Scheme 4). Their interactions with the *N*-substituent may contribute to the observed diastereoselection which corresponds to ΔG *ca.* 2.1 kJ mol^{-1}. The cyclisation of the preferred conformer generates (**3b**) in which the ethyl chain is axial. This major product results from kinetic control and is certainly less stable than (**3a**) which possesses an equatorial ethyl chain; therefore the 40% value of diastereoisomeric excess is the minimum possible value.



Scheme 4.

However, no direct proof of the relative stability of (**3a**, **b**) can be produced since the equilibrium of pure (**3a**) and pure (**3b**) in a weak acidic medium affords, respectively and quantitatively, their *cis*-isomers (**4a**, **b**) (Scheme 1). The *trans–cis* isomerisation occurs *via* the conjugate enol (**8**), the formation of which involves abstraction of the axial benzylic H(4a), which is more acidic than H(3).[18,19] Alkylation of the (**3a**) + (**3b**) mixture (30:70) gives stereospecifically *cis*-4a-substituted compounds (**5a**) + (**5b**) (30:70). The reaction occurs *via* the enolate (**9**)



(**8**) M = H
(**9**) M = K

without epimerisation of the side chain since 4a-alkylated compounds are exclusively obtained and the ratio of (**5a**):(**5b**) remains unchanged compared with the (**3a**) + (**3b**) mixture. Equilibrium between (**5a**) and (**5b**) can however be realised in strongly acidic conditions.

Starting from either (**5a**) + (**5b**) (30:70) or pure (**5a**) or (**5b**), the ratio of compounds in the mixture obtained is always 50:50;

this corresponds to the thermodynamic equilibrium and shows that (**5a**) and (**5b**) have the same free enthalpy.

These results demonstrate the higher stability of the *cis*-stereochemistry in hexahydrocarbazolones as observed previously in an analogous series[16] and in 8-methylhydrindanes.[14]

Conclusions

Photocyclisation of aryl enaminones gives exclusively hexahydrocarbazol-4-ones with a *trans*-ring junction, even in molecules having a C(3) substituent; this latter introduces important diastereoselection (40% minimum).

cis-Isomers are much more stable than the corresponding *trans*-isomers. They are obtained exclusively by equilbration without modification of the C(3) centre. Alkylation, in the presence of KH, affords regio- and stereo-specifically, *cis*-4a-substituted derivatives, even with compounds having a 3-ethyl group. This result is of interest since the *cis*-relationship of the B/C ring junction is the stereochemistry adopted by many natural pentacyclic indole alkaloids.

Full interpretation of ^{1}H (1D, 2D) NMR spectra allows the conformation of the C ring to be established in all of the compounds studied; thus, the C ring adopts nearly a chair form in *trans*-derivatives and a flattened chair form in *cis*-derivatives.

Molecular-model calculations of these molecules are in progress.

Experimental

Irradiations were performed in a Pyrex glass vessel using a medium-pressure mercury lamp (Philips, 400 W). Melting points were determined using a Reichert hot-stage microscope and are uncorrected. Mass spectra were obtained at 70 eV using a Varian CH-5 spectrometer. Infrared spectra were run on a Perkin–Elmer 377 spectrophotometer. ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded at 20 °C on a Bruker MSL-300 spectrometer and were obtained for $CDCl_3$ solutions (0.1–0.3 mol dm^{-3}) with the deuterium signal as an internal lock. The following conditions were used:

(1*D*) ^{1}*H NMR*. Resonance frequency, 300 MHz; number of scans, 50–150; pulse repetition time 4 s; acquisition time 2 s; spectral width 3 000 Hz; digital resolution, 0.3 Hz/pt.

COSY. Applied pulse sequence [90°–t_1–45°–FID (t_2)]; spectral width in F_1 and F_2, 1 200 Hz; number of scans, 96.

^{13}*C NMR* (*BB and* J-*modulated echo spectra*). Resonance frequency 75.4 MHz; number of scans 500–1 500; pulse repetition time 4 s; acquisition time, 1 s; spectral width, 18 000 MHz; digital resolution, 2 Hz/pt.

Enaminones (**1**) *and* (**2**).—These compounds were prepared according to the literature method.[7]

trans-*Hexahydrocarbazol-4-ones* (**3a**) *and* (**3b**).—A degassed solution of (**2**) (2.7 g, 8.85 mmol) in benzene (500 cm^3) was irradiated for 50 min under an atmosphere of argon. Evaporation of the solvent gave crude material of a mixture of compounds (**3a**) and (**3b**) (ratio 30:70) which could be separated by flash chromatography with hexane–ethyl acetate (97:3) as the eluant (84% yield).

Compound (**3a**): m.p. 132–134 °C (from hexane–ethyl acetate 90:10) (Found: $M^{+\cdot}$, 305.1770. $C_{21}H_{23}NO$ requires M, 305.1774); m/z (EI) 305 (26%), 275 (60), 248 (46), 218 (30), and 91 (100); $\nu_{max}(CCl_4)$ 1 720 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 11.9 (CH_3), 21.6, 29.8, 30.8 (CH_2), 51.7 (CH), 52.8 (CH_2), 58.0, 74.0 (CH), 108.9, 119.4, 124.9 (=CH), 125.5 (=C), 127.1, 127.5, 127.8, 128.5 (=CH), 138.7, 153.1 (=C), and 206.2 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

Compound (**3b**): m.p. 126–128 °C (from hexane–ethyl acetate 90:10) (Found: $M^{+\cdot}$, 305.1773. $C_{21}H_{23}NO$ requires M, 305.1 774); m/z (EI) 305 (32%), 275 (58), 248 (47), 218 (27), and 91 (100); $\nu_{max}(CCl_4)$, 1 720 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 12.0 (CH_3), 25.5, 25.9, 27.7 (CH_2), 51.4 (CH), 52.7 (CH_2), 54.0. 72.3 (CH), 108.9, 119.4, 124.9 (=CH), 125.3 (=C), 127.2, 127.6, 127.9, 128.5 (=CH), 138.7, 152.9 (=C), and 208.8 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

cis-*Hexahydrocarbazol-4-ones* (**4a**) *and* (**4b**).—A solution of (**2a**) [or (**2b**)] (30 mg, 0.1 mmol) in CH_2Cl_2 (3 cm^3) containing a catalytic amount of (±)camphor-10-sulphonic acid (1 mg) was refluxed for 5 h. The reaction mixture was then neutralised at room temperature with anhydrous K_2CO_3. After filtration and concentration of the organic phase, compound (**4a**) [or (**4b**)] was purified by flash chromatography with hexane–ethyl acetate (95:5) as the eluant (90% yield).

Compound (**4a**): m.p. 128–130 °C (from hexane–ethyl acetate, 90:10) (Found: $M^{+\cdot}$, 305.1776. $C_{21}H_{23}NO$ requires M, 305.1774); m/z (EI) 305 (28%), 275 (61), 248 (50), 218 (24), and 91 (100); $\nu_{max}(CCl_4)$ 1 700 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 11.4 (CH_3), 22.6, 24.3, 25.4 (CH_2), 48.8 (CH), 50.1 (CH_2), 54.8, 66.1 (CH), 107.6, 118.2, 124.5 (=CH), 126.9 (=C), 127.3, 127.6, 127.9, 128.8 (=CH), 138.1, 150.9 (=C), and 210.9 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

Compound (**4b**): m.p. 129–131 °C (from hexane–ethyl acetate, 90:10) (Found: $M^{+\cdot}$, 305.1771. $C_{21}H_{23}NO$ requires M, 305.1774); m/z (EI) 305 (30%), 275 (57), 248 (54), 218 (30), and 91 (100); $\nu_{max}(CCl_4)$ 1 700 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 11.7 (CH_3), 23.3, 24.9, 25.3 (CH_2), 51.1 (CH), 51.2 (CH_2), 54.2, 66.0 (CH), 107.9, 118.3 (=CH), 126.2 (=C), 126.4, 127.1, 127.2, 127.6, 128.6 (=CH), 138.7, 152.4 (=C), and 210.7 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

4a-*Methyl*-cis-*hexahydrocarbazol-4-ones* (**5a**) *and* (**5b**).—Those compounds were prepared according to the method already described,[16] *i.e.*, by the alkylation of *trans*-hexahydrocarbazol-4-ones (**3a**) + (**3b**), with KH (1.1 equiv.) and methyl iodide (1.1 equiv.) (ratio 30:70). The isomers were separated by flash chromatography with hexane–ethyl acetate (95:5) as the eluant (80% yield).

Compound (**5a**): (Found: $M^{+\cdot}$, 319.1934. $C_{22}H_{25}NO$ requires M, 319.1936; m/z (EI) 319 (38%), 291 (15), 234 (21), 220 (10), 200 (19), and 91 (100); $\nu_{max}(CCl_4)$, 1 700 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 11.4 (CH_3), 22.7 (CH_2), 23.0 (CH_3), 24.0, 26.1 (CH_2), 46.9 (CH), 50.1 (CH_2), 57.2 (C), 73.9 (CH), 107.4, 118.1, 123.3, 127.2, 127.4, 128.6, 128.7 (=CH), 132.2, 138.4, 150.4 (=C), and 212.4 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

Compound (**5b**): (Found: $M^{+\cdot}$, 319.1934. $C_{22}H_{25}NO$ requires M, 319.1936; m/z (EI) 319 (22%), 291 (16), 234 (28), 220 (10), 200 (19), and 91 (100); $\nu_{max}(CCl_4)$, 1 700 cm^{-1} (CO); δ_C(300 MHz; $CDCl_3$) 11.7, 23.6 (CH_3), 23.7, 24.4, 25.5 (CH_2), 49.3 (CH), 51.1 (CH_2), 56.8 (C), 73.4 (CH), 107.8, 118.3, 125.2, 127.1, 127.3, 128.5, 128.7 (=CH), 131.6. 138.8, 151.8 (=C), and 213.8 (CO); the ^{1}H NMR data are shown in Tables 1 and 2.

Equilibration reactions between (**5a**) and (**5b**) were performed by heating a benzene solution of either the alkylation mixture (**5a**) + (**5b**) (30:70) or the pure compound (**5a**) or (**5b**) in presence of a catalytic amount of (±)-camphor-10-sulphonic acid and few drops of ethanol.

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