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Entropy-Controlled Diastereoselectivity in the Photocyclization of Rigid Derivatives of *o*-Allylaniline

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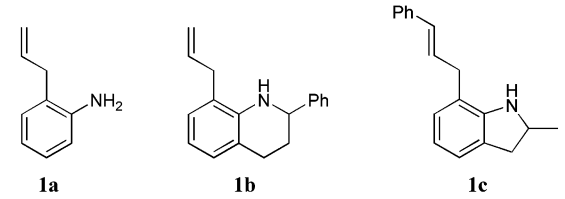
Abstract: Two rigid derivatives of *o*-allylaniline, namely 8-allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (**1b**) and 7-(*trans*-2-cinnamyl)-2-methylindoline (**1c**), have been chosen as suitable systems to study the potential stereoselectivity of the photocyclization process. Photolysis of **1b** leads to a mixture of diastereomeric lilolidines **4** (*trans*/*cis*), while **1c** produces a mixture of **4** (*trans*/*cis*) and the tetrahydropyrrolo[3,2,1-*hi*]indole derivatives **5** (*trans*/*cis*). To disclose whether the diastereoselectivity could be entropy dependent, photolysis of **1b** and **1c** has been performed at several temperatures. In both cases, linear relationships have been observed when $\ln(k_t/k_c)$ (the relative reaction rate constants calculated from the diastereomeric excess) is plotted against the reciprocal temperatures. However, significant entropy-controlled diastereoselectivity has only been found for the photocyclization of **1c** to **4**. The fluorescence spectra of **1b**,**c** show formation of intramolecular charge-transfer exciplexes, which is in agreement with the proposed excited-state electron-transfer mechanism for photocyclization.

Chiral compounds are in high demand in a number of fields, including the development of new pharmaceuticals. This has led to considerable efforts aimed at producing novel chemistry based on asymmetric methodologies.[1−3] In this context, photochemical reactions have been shown to be particularly promising for achieving a multidimensional stereochemical control by the combined use of the entropy-related factors, pressure and solvent.[4−6]

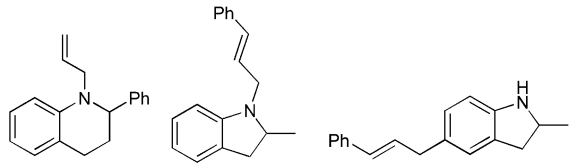
Being essentially independent from temperature restrictions, photochemical reactions are advantageous for studying the entropy effects on stereoselectivity. Thus, early work on the Paterno−Buchi photocycloaddition with optically active carbonyl compounds has shown that the diastereoselectivity of the resulting oxetanes is temperature dependent.[7] Later, a clear temperature effect has been observed in a number of enantio- and diastereodifferentiating photoprocesses.[5,6]

CHART 1



1a **1b** **1c**

CHART 2



2b **2c** **3c**

In many cases, the mechanism of stereoselective photoreactions is thought to involve formation of exciplexes.[5,6] Conformational locking by increasing the rigidity of the systems may enhance exciplex geometries leading to stereodifferentiating photoreactions.[6] In this context, the introduction of bulky substituents can be used as a convenient tool to enhance stereoselectivity.

In the present work, two rigid derivatives of *o*-allylaniline (**1a**), namely 8-allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (**1b**) and 7-(*trans*-2-cinnamyl)-2-methylindoline (**1c**), have been chosen as suitable systems to study the potential stereoselectivity of the photocyclization processes (Chart 1). It is known that irradiation of **1a** leads to formation of a *5*-membered ring product via intramolecular excited-state electron transfer.[8] Some of its analogues exhibit emission spectra which have been tentatively assigned to intramolecular exciplexes.[8d,9] A simplified mechanism for the photocyclization of *o*-allylanilines is shown in Scheme 1. Compounds **1b** and **1c** possess a chiral carbon atom, due to substitution at C-2; this would allow in both cases formation of two diastereoisomers upon cyclization. Besides, phenyl substitution at the end of the allylic side chain in **1c** provides a new light-absorbing chromophore (the styrene chromophore) and makes possible photocyclization to six-membered-ring compounds. Furthermore, the five-mem-

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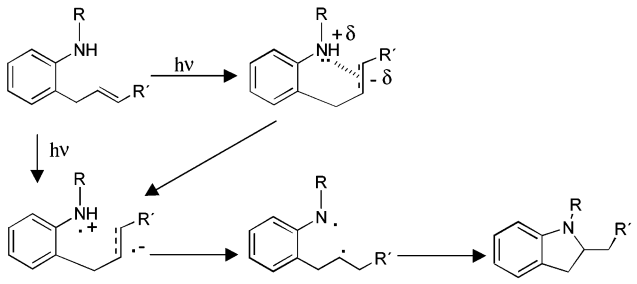
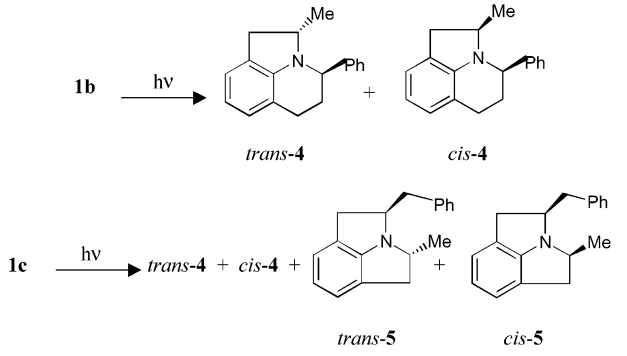
SCHEME 1



SCHEME 2



bered-ring products obtained from **1b** would be identical with the six-membered-ring products arising from **1c**; this could allow one to compare the possible diastereoselectivities (if any) and to relate them to the structures of the starting materials and to the nature of the ring being formed, rather than to the stability of the final products. It will be shown that, at least in the case of **1c**, the diastereoselectivity is entropy controlled, as indicated by the temperature effect; besides, exciplex emission is clearly observed in the fluorescence spectra of the two compounds.

The required substrates **1b** and **1c** were prepared in two steps: (i) treatment of 2-phenyl-1,2,3,4-tetrahydroquinoline or 2-methylindoline with allyl bromide or cinnamyl chloride, respectively, and (ii) amino-Claisen rearrangement of the resulting *N*-substituted derivatives **2b**,**c** in the presence of zinc chloride, using refluxing *p*-xylene or bromobenzene as solvent. In the case of **2c**, rearrangement gave also 5-(*trans*-2-cinnamyl)-2-methylindoline (**3c**) as byproduct.

Photolysis of **1b** and **1c** was performed in a multilamp photoreactor, at 254 and 300 nm, in both hexane and acetonitrile. The results for **1b** are shown in Table 1, entries 1−4. The reaction was clean, leading to a mixture of diastereomeric lilolidines **4**. The relative arrangement of the substituents (trans or cis) was unambiguously determined by means of NOE measurements. In general, the trans isomer was slightly favored, particularly in the shorter wavelength irradiation experiments. Although the yields are moderate, this constitutes a direct entry to the lilolidine ring system, which is present in the structure of some natural alkaloids with potent antifungal properties.[10] When **1c** was photolyzed, a mixture of **4** (*trans*/*cis*) and the tetrahydropyrrolo[3,2,1-*hi*]indole derivatives **5** (*trans*/*cis*) was obtained (Table 1, entries 5−8). Stereochemical assignment of the latter was achieved by NOE experiments, as in the case of **4**. In acetonitrile, the photocyclization was regioselective, to give **4** as the only products. Again, some diastereoselectivity was observed in the photocyclization; for the lilolidines this effect was slightly higher when using the shorter wavelength lamps.

TABLE 1. Photochemistry of Compounds 1b and 1c

entry	compd	cond.[a]	conv.[b]	mass balance	products (%)			
					trans-**4**	*cis*-**4**	*trans*-**5**	*cis*-**5**
1	**1b**	A	71	97	54	46		
2		B	63	99	51	49		
3		C	65	87	53	47		
4		D	61	90	49	51		
5	**1c**	A	71	72	42	37	11	10
6		B	69	55	34	32	16	18
7		C	96	73	47	53		
8		D	72	61	48	52		

[a] Irradiations were carried out in a multilamp photoreactor at 254 nm (A and C) or 300 nm (B and D). Deoxygenated solutions of hexane (A and B) or acetonitrile (C and D) were employed. Irradiation time was always 30 min. [b] Conversion degrees, mass balances, and product distributions were determined by gas chromatography using adequate standards.

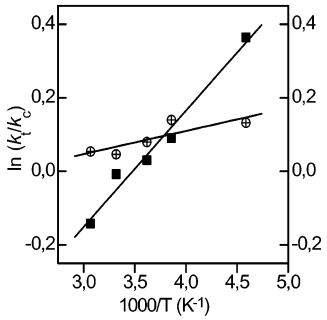


FIGURE 1. Temperature effect on the de (diastereomeric excess) in the photocyclization of **1b** (⊕) and **1c** (■) to *trans*-**4** and *cis*-**4** in an immersion well photoreactor, with the quartz-filtered light of a medium-pressure Hg lamp, using pentane as solvent; k_t/k_c = (100 + % de)/(100 − % de). Conversion degrees were about 80%.

For comparison, the cyclization of **1b**,**c** was also carried out by means of HBr in acetic acid, at 70 (**1b**) or 120 °C (**1c**). The only products were in both cases *trans*/*cis*-**4**, with a ca. 1:1 diastereomeric ratio.

All the data in Table 1 were obtained at room temperature. To disclose whether the diastereoselectivity could be entropy dependent, photolysis of **1b** and **1c** was performed at several temperatures. The results are shown in Figure 1. In both cases, linear relationships were observed when $\ln(k_t/k_c)$ (the relative reaction rate constants calculated from the diastereomeric excess) was plotted against the reciprocal temperatures. According to the modified Arrhenius and Eyring equation (eq 1), the activation parameters can be determined from the slopes and intercepts of the regression lines.[6]

$$\ln(k_t/k_c) = \Delta E_{t-c}/RT + \ln(A_t/A_c) = -\Delta\Delta H^{\ddagger}_{t-c}/RT + \Delta\Delta S^{\ddagger}_{t-c}/R \quad (1)$$

As shown in Figure 1, significant entropy-controlled diastereoselectivity was only found for the photocycliza-

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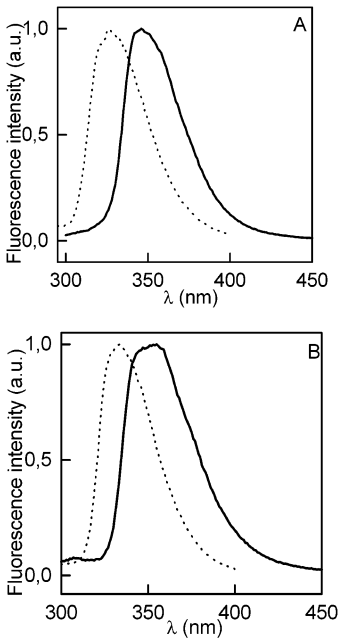

FIGURE 2. (A) Fluorescence spectra of **1b-H** (···) and **1b** (—). (B) Fluorescence spectra of **1c-H** (···) and **1c** (—).

tion of **1c** to **4**. The corresponding differential enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy ($\Delta\Delta S^{\ddagger}$) of activation were found to be −0.62 kcal mol^{-1} and −2.18 cal mol^{-1} K^{-1}, respectively. The equipodal temperature (292 K) is very close to room temperature, which explains the low diasteroselectivities given in Table 1. However, it is very remarkable that changing the temperature allows one to increase the diastereoselectivity and even to obtain predominantly the *trans*- or the *cis*-lilolidines.

After performing the product studies, the photophysical properties of **1b**,**c** were examined to gain further insight into the mechanistic aspects. The most salient features of the fluorescence spectra are depicted in Figure 2. For comparison, the figure also shows the fluorescence spectra of **1b-H** and **1c-H**, obtained by catalytic hydrogenation of **1b** and **1c**, respectively. These compounds lack the olefin moiety and cannot form intramolecular exciplexes.

As shown in panel A, the emission of **1b** in hexane is red-shifted (ca. 20 nm) with respect to the reference compound **1b-H**. A similar red shift was observed under the same conditions when comparing the emission spectra of **1c** and **1c-H** (panel B). Thus, the fluorescence spectra of **1b**,**c** in hexane can be safely attributed to formation of intramolecular charge-transfer exciplexes.[8d,9] This effect is also observed in acetonitrile (data not shown), although the changes associated with exciplex formation are less marked.

In summary, photocyclization of the rigid *o*-allylaniline derivatives **1b** and **1c** occurs with remarkable regioselectivity, giving the lilolidines **4** as the only (or major) photoproducts. Intramolecular charge-transfer exciplexes are detected in both hexane and acetonitrile, which is in agreement with the proposed excited-state electron-transfer mechanism for the photocyclization of *o*-allylanilines. Although diastereoselectivity is observed only to a limited extent at room temperature, in the case of **1c** it can be temperature controlled to give predominantly the trans or the cis isomers, at will. The linear relationships obtained when plotting $\ln(k_t/k_c)$ against the reciprocal temperature have allowed an estimatation of the activation parameters for this process.

Experimental Section

FTIR spectra were obtained in liquid films or (in the case of **1b** and **1c**) in CCl_4 solution; ν_{max} (cm^{-1}) is given for the significant absorption bands. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 or 75 MHz, respectively; chemical shifts are reported in δ (ppm) values, using TMS as internal standard. Mass spectra were obtained under electron impact; the ratios *m*/*z* and the relative intensities (%) are indicated for the significant peaks.

Preparation of the Substrates. 1-Allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (**2b**) was prepared by reaction between 2-phenyl-1,2,3,4-tetrahydroquinoline[11] and allyl bromide in the presence of K_2CO_3 with acetone as solvent, following a previously described method.[8c] 1-(*trans*-2-Cinnamyl)-2-methylindoline (**2c**) was prepared by reaction between 2-methylindoline and cinnamyl chloride in the presence of NaOH with dimethyl sulfoxide as solvent, as reported in the literature for related compounds.[12] **1b** was prepared by amino-Claisen rearrangement of 1-allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (**2b**) with $ZnCl_2$ and *p*-xylene at 140 °C, using the standard method.[13] Similarly, amino-Claisen rearrangement of 1-(*trans*-2-cinnamyl)-2-methylindoline (**2c**) with $ZnCl_2$, using bromobenzene at 150 °C, leads to 5-(*trans*-2-cinnamyl)-2-methylindoline (**3c**) as the major product (42%) and 7-(*trans*-2-cinnamyl)-2-methylindoline (**1c**) as the minor product (9%). Hydrogenation of **1b** and **1c** was performed as usual, with Pd/C (10%) as the catalyst and ethyl acetate as solvent. The corresponding products **1b-H** and **1c-H** were obtained in quantitative yields.

Irradiation Procedure. Solutions of **1b** or **1c** (5 mM) in the indicated solvent were irradiated in quartz or Pyrex tubes surrounding a centrally positioned quartz cooling jacket containing a 125-W medium-pressure Hg lamp or inside a multilamp photoreactor, using the light from four 8W lamps with emission maxima at λ = 254 or 300 nm (Gaussian distribution). The course of the reaction was followed by GC, GC-MS, and ^{1}H NMR; the degrees of conversion, mass balances, and product distributions were determined using adequate standards. Isolation and purification were carried out by conventional column chromatography on silica gel Merck 60 (0.063−0.200 mm), using hexane/ethyl acetate or hexane/dicloromethane as eluent.

8-Allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (1b): FTIR 3438, 3396, 1635, 1599, 1491, 1469, 1315, 1267; ^{1}H NMR 1.84−2.20 (m, 2H), 2.68−2.78 (dt, J_1 = 16.3 Hz, J_2 = 4.7 Hz, 1H), 2.87−3.00 (ddd, J_1 = 16.3 Hz, J_2 = 10.5 Hz, J_3 = 5.3 Hz, 1H), 3.25 (d, J = 6.1 Hz, 2H), 4.08 (s, 1H), 4.47 (dd, J_1 = 9.1 Hz, J_2 = 3.1 Hz, 1H), 5.01−5.10 (m, 2H), 5.87−6.01 (m, 1H), 6.64 (t, J = 7.4 Hz, 1H), 6.92 (d, J = 7.4 Hz, 2H), 7.22−7.40 (m, 5H); ^{13}C NMR 26.7 (CH_2), 30.9 (CH_2), 36.2 (CH_2), 56.3 (CH), 116.3−136.0 (CH_2, CH, and C), 142.7 (C), 145.1 (C); MS 249 (M^+, 100), 248 (28), 172 (73), 145 (25), 130 (21), 91 (12), 77 (8). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1525.

2-Phenyl-8-propyl-1,2,3,4-tetrahydroquinoline (1b-H): FTIR 3437, 1599, 1491, 1468, 754, 700; ^{1}H NMR 0.90 (t, J = 7.3 Hz, 3H), 1.58 (m, 2H), 1.82−2.11 (m, 2H), 2.32 (t, J = 7.5 Hz, 2H), 2.62−2.95 (m, 2H), 3.90 (br s, 1H), 4.40 (dd, J_1 = 9.3 Hz, J_2 = 3.3 Hz, 1H), 6.54 (t, J = 7.4 Hz, 1H), 6.83 (m, 2H), 7.19−7.35 (m, 5H); ^{13}C NMR 14.3 (CH_3), 21.6 (CH_2), 26.8 (CH_2), 31.1 (CH_2), 33.1 (CH_2), 56.5 (CH), 116.5 (CH), 120.5−128.6 (CH and C), 142.1 (C), 145.3 (C); MS 251 (M^+, 100), 250 (25), 222 (73), 207 (8), 174 (41), 130 (11), 91 (10). Exact mass calcd for $C_{18}H_{21}N$ 251.1674, found 251.1669.

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7-(*trans*-2-Cinnamyl)-2-methylindoline (1c): FTIR 3382, 1602, 1477, 1458; ^{1}H NMR 1.26 (d, J = 6.2 Hz, 3H), 2.64 (dd, J_1 = 15.5 Hz, J_2 = 7.7 Hz, 1H), 3.16 (dd, J_1 = 15.5 Hz, J_2 = 8.5 Hz, 1H), 3.40 (d, J = 6.0 Hz, 2H), 3.78 (br s, 1H), 3.96 (m, 1H), 6.27−6.36 (dt, J_1 = 15.8 Hz, J_2 = 6.0 Hz, 1H), 6.45 (d, J = 15.8 Hz, 1H), 6.69 (t, J = 7.4 Hz, 1H), 6.91 and 7.00 (d + d, J = 7.4 Hz, 1H + 1H), 7.20−7.39 (m, 5H); ^{13}C NMR 22.4 (CH_3), 35.3 (CH_2), 37.8 (CH_2), 55.1 (CH), 118.8 (CH), 120.4 (CH), 122.9−130.9 (CH and C), 137.3 (C), 149.6 (C); MS 249 (M^+, 100), 234 (61), 130 (38), 117 (97), 91 (19). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1512.

2-Methyl-7-(3-phenylpropyl)indoline (1c-H): FTIR 3377, 1601, 1456, 746, 700; ^{1}H NMR 1.22 (d, J = 6.2 Hz, 3H), 1.83−2.78 (m, 7H), 3.07 (dd, J_1 = 15.5 Hz, J_2 = 8.6 Hz, 1H), 3.90 (m, 1H), 6.60 (t, J = 7.4 Hz, 1H), 6.80 and 6.88 (d + d, J = 7.4 Hz, 1H + 1H), 7.09−7.29 (m, 5H); ^{13}C NMR 22.2 (CH_3), 29.7 (CH_2), 30.5 (CH_2), 35.5 (CH_2), 37.9 (CH), 55.1 (CH), 117.5−142.0 (CH and C); MS 251 (M^+, 100), 236 (76), 207 (12), 147 (71), 130 (36), 118 (22), 91 (65). Exact mass calcd for $C_{18}H_{21}N$ 251.1674, found 251.1670.

1-Allyl-2-phenyl-1,2,3,4-tetrahydroquinoline (2b): FTIR 1602, 1498, 744; ^{1}H NMR 2.00−2.22 (m, 2H), 2.53−2.60 (dd, J_1 = 7.5 Hz, J_2 = 4.4 Hz, 2H), 3.58 and 4.06 (m + m, 2H), 4.59 (t, J = 7.4 Hz, 1H), 5.08−5.20 (m, 2H), 5.75−5.84 (m, 1H), 6.60 (t, J = 7.3 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 6.97 (d, J = 7.3 Hz, 1H), 7.09 (m, 1H), 7.16−7.32 (m, 5H); ^{13}C NMR 23.8 (CH_2), 29.6 (CH_2), 51.7 (CH_2), 60.7 (CH), 110.3 (CH), 115.4−133.4 (CH_2, CH and C), 144.3 (C), 144.9 (C); MS 249 (M^+, 96), 222 (16), 208 (32), 172 (100), 144 (14), 130 (41), 91 (29), 77 (12). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1519.

1-(*trans*-2-Cinnamyl)-2-methylindoline (2c): FTIR 1604, 1483, 746; ^{1}H NMR 1.32 (d, J = 6.1 Hz, 3H), 2.63 (dd, J_1 = 15.4 Hz, J_2 = 9.8 Hz, 1H), 3.12 (dd, J_1 = 15.4 Hz, J_2 = 8.5 Hz, 1H), 3.66−4.04 (m, 3H), 6.20−6.31 (ddd, J_1 = 15.8 Hz, J_2 = 7.0 Hz, J_3 = 4.8 Hz, 1H), 6.50 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 15.8 Hz, 1H), 6.65 (t, J = 7.3 Hz, 1H), 7.04 (m, 2H), 7.16−7.39 (m, 5H); ^{13}C NMR 19.4 (CH_3), 37.3 (CH_2), 48.7 (CH_2), 59.9 (CH), 107.1 (CH), 117.5 (CH), 124.1−131.7 (CH and C), 136.9 (C), 152.2 (C); MS 249 (M^+, 48), 234 (10), 130 (5), 117 (100), 91 (15). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1507.

5-(-*trans*-2-Cinnamyl)-2-methylindoline (3c): FTIR 3371, 1616, 1491, 1450, 1250; ^{1}H NMR 1.25 (d, J = 6.2 Hz, 3H), 2.57 (dd, J_1 = 15.5 Hz, J_2 = 7.9 Hz, 1H), 3.08 (dd, J_1 = 15.5 Hz, J_2 = 8.4 Hz, 1H), 3.41 (d, J = 6.1 Hz, 2H), 3.52 (br s, 1H), 3.93 (m, 1H), 6.26−6.38 (dt, J_1 = 15.7 Hz, J_2 = 6.1 Hz, 1H), 6.41 (d, J = 15.7 Hz, 1H), 6.52 (d, J = 7.9 Hz, 1H), 6.86 (d, J = 7.9 Hz, 1H), 6.94 (s, 1H), 7.12−7.37 (m, 5H); ^{13}C NMR 22.2 (CH_3), 37.7 (CH_2), 38.8 (CH_2), 55.4 (CH), 109.1 (CH), 125.0−130.3 (CH and C), 137.6 (C), 149.3 (C); MS 249 (M^+, 100), 234 (61), 130 (38), 117 (97), 91 (19). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1515.

***trans*-2-Methyl-4-phenyl-1,2,5,6-tetrahydro-4*H*-pyrrolo-[3,2,1-*ij*]quinoline (*trans*-4):** FTIR 1601, 1471, 1365; ^{1}H NMR 1.00 (d, J = 6.3 Hz, 3H), 1.99−2.24 (m, 2H), 2.49−2.83 (m, 3H), 3.14 (dd, J_1 = 15.3 Hz, J_2 = 8.5 Hz, 1H), 3.68−3.80 (m, 1H), 4.31 (dd, J_1 = 7.8 Hz, J_2 = 3.5 Hz, 1H), 6.57 (t, J = 7.3 Hz, 1H), 6.83 and 6.93 (d + d, J = 7.3 Hz, 1H + 1H), 7.23−7.37 (m, 5H); ^{13}C NMR 16.9 (CH_3), 23.4 (CH_2), 32.6 (CH_2), 36.7 (CH_2), 56.1 (CH), 56.7 (CH), 116.9 (CH), 117.9 (CH), 122.4−128.4 (CH and C), 142.6 (C), 148.2 (C); MS 249 (M^+, 77), 248 (4), 234 (100), 172 (31), 130 (30), 117 (52), 77 (6). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1509.

***cis*-2-Methyl-4-phenyl-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline (*cis*-4):** FTIR 1601, 1479, 1346; ^{1}H NMR 0.86 (d, J = 6.1 Hz, 3H), 1.89−2.20 (m, 2H), 2.49−2.70 (m, 3H), 3.04 (dd, J_1 = 15.7 Hz, J_2 = 8.0 Hz, 1H), 3.60 (m, 1H), 3.99 (dd, J_1 = 5.8 Hz, J_2 = 4.6 Hz, 1H), 6.61 (t, J = 7.3 Hz, 1H), 6.85 and 6.94 (d + d, J = 7.3 Hz, 1H + 1H), 7.23−7.37 (m, 5H); ^{13}C NMR 15.3 (CH_3), 22.8 (CH_2), 31.6 (CH_2), 38.2 (CH_2), 64.1 (CH), 65.8 (CH), 117.5 (CH), 119.0 (CH), 121.6 (CH), 125.8−128.1 (CH and C), 145.5 (C), 149.9 (C); MS 249 (M^+, 79), 248 (6), 247, (3), 234 (100), 172 (32), 130 (31), 117 (54), 77 (6). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1512.

***trans*-2-Benzyl-4-methyl-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (*trans*-5):** FTIR 1591, 1475, 1454, 750, 700; ^{1}H NMR 0.84 (d, J = 6.5 Hz, 3H), 2.73 (dd, J_1 = 15.1 Hz, J_2 = 3.5 Hz, 1H), 2.85 (dd, J_1 = 13.5 Hz, J_2 = 7.3 Hz, 1H), 2.98−3.28 (m, 3H), 3.43 (dd, J_1 = 15.1 Hz, J_2 = 7.7 Hz, 1H), 3.78 (m, 1H), 4.01 (m, 1H), 6.55 (t, J = 7.2 Hz, 1H), 6.84 (m, 2H), 7.16−7.33 (m, 5H); ^{13}C NMR 16.3 (CH_3), 40.5 (CH_2), 40.7 (CH_2), 42.2 (CH_2), 60.2 (CH), 65.7 (CH), 119.4−129.6 (CH and C), 139.7 (C); MS 249 (M^+, 8), 158 (100), 130 (19), 117 (21), 91 (8). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1518.

***cis*-2-Benzyl-4-methyl-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]-indole (*cis*-5):** FTIR 1591, 1471, 1340, 1279, 750, 700; ^{1}H NMR 1.42 (d, J = 6.2 Hz, 3H), 2.90−3.28 (m, 6H), 3.40−3.61 (m + m, 1H + 1H), 6.57 (t, J = 7.2 Hz, 1H), 6.78 and 6.84 (d + d, J = 7.2 Hz, 1H + 1H), 7.17−7.33 (m, 5H); ^{13}C NMR 21.1 (CH_3), 41.2 (CH_2), 42.2 (CH_2), 43.6 (CH_2), 69.1 (CH), 74.4 (CH) 120.3−129.4 (CH and C), 139.2 (C); MS 249 (M^+, 9), 158 (100), 130 (18), 117 (21), 91 (8). Exact mass calcd for $C_{18}H_{19}N$ 249.1517, found 249.1512.

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and GC-MS spectra of compounds **1b**,**c**, **1b-H**, **1c-H**, **2b**,**c**, **3c**, **4** (*trans*/*cis*), and **5** (*trans*/*cis*); relevant NOE effects for the assignment of **4** (*trans*/*cis*) and **5** (*trans*/*cis*). This material is available free of charge via the Internet at http://pubs.acs.org.

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