Synthesis and conformational analysis of 2-amino-1,2,3,4-tetrahydro-1-naphthalenols[1]

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Received March 31, 1987[3]

ANTONIO DELGADO, JOSÉ MIGUEL GARCIA, DAVID MAULEON, CRISTINA MINGUILLON, JOAN RAMON SUBIRATS, MIGUEL FELIZ, FRANCISCO LOPEZ, and DOLORES VELASCO. Can. J. Chem. **66**, 517 (1988).

Synthesis and conformational analysis of several *cis*- and (or) *trans*-2-amino-1,2,3,4-tetrahydro-1-naphthalenols are described. Introduction of the nitrogen atom at the C(2) position of the starting tetralones **3** has been carried out through nitrosation followed by reduction of the intermediate hydroxyimino tetralone and (or) Neber rearrangement of the tosyloxy derivatives **7***a–e*. Stereoselective reduction of the C(1) carbonyl group of acetamidotetralones **5***a–e* or aminotetralones **8***a–e* afforded the corresponding acetamido or aminotetralols, respectively, of OH/N *trans* stereochemistry whereas an opposite stereoselectivity was observed in reduction of C(8)-OCH_3 derivatives **5***f* and **8***f* under the same experimental conditions. Finally, acid hydrolysis of *trans*-acetamidotetralols led to *cis*-aminoalcohols in high yields. Conformational analysis has been carried out by ^1H nuclear magnetic resonance techniques and MM2 theoretical calculations. All *cis* derivatives showed a major conformation in which the C(1)-OH group adopts a pseudoaxial disposition. On the other hand, *trans*-aminoalcohols in $CDCl_3$ showed a major or exclusive OH/N *trans*-dipseudoequatorial conformation in which stabilization by intramolecular OH/N hydrogen bonding is possible. The only exception was found in C(8)-OCH_3 *trans*-aminoalcohols in DMSO-d_6 solution, which showed a major OH/N *trans*-diaxial conformation.

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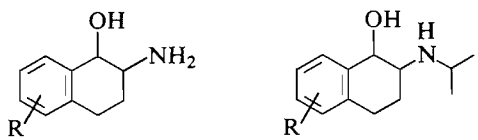
On décrit la synthèse et l'analyse conformationnelle de plusieurs amino-2 tétrahydro-1,2,3,4 naphtalénols-1-*cis* et -*trans*. Pour introduire un atome d'azote en position C(2) des tétralones **3** de départ, on a fait appel soit à une nitrosation suivie d'une réduction de l'hydroximino tétralone intermédiaire soit à une transposition de Neber des dérivés tosyloxy **7***a–e*. La réduction stéréosélective du groupement carbonyle en C(1) des acétamidotétralones **5***a–e* ou des aminotétralones **8***a–e* conduit aux acétamido ou aminotétralols correspondants de stéréochimie OH/N *trans*; par ailleurs, on obtient la stéréochimie inverse lorsqu'on réduit les dérivés C(8)-OCH_3, **5***f* et **8***f*, en utilisant les mêmes conditions expérimentales. Enfin, l'hydrolyse acide des acétamidotétralols-*trans* conduit au aminoalcools-*cis*, avec d'excellents rendements. On a réalisé l'analyse conformationnelle à l'aide de la résonance magnétique nucléaire du ^1H et de calculs théoriques MM2. Pour chacun des dérivés *cis*, la conformation prédominante comporte un groupement C(1)-OH dans une position pseudo-axiale. Par ailleurs, en solution dans le $CDCl_3$, les aminoalcools *trans* présentent une conformation majeure, sinon exclusive, OH/N di-pseudo-équatoriale *trans* dans laquelle une stabilisation par liaison OH/N intramoléculaire est possible. On a noté une seule exception; il s'agit des aminoalcools *trans* C(8)-OCH_3 qui, en solution dans le DMSO-d_6, existent dans une conformation OH/N *trans*-diaxiale.

[Traduit par la revue]

As part of our research concerning the synthesis of conformationally restrained arylethanolamines, this paper deals with the synthesis and conformational analysis of several *cis*- and (or) *trans*-2-amino-1,2,3,4-tetrahydro-1-naphthalenols **1***a–i* and **2***a–i* (Scheme 1) as potential adrenergic agents.

In all cases, synthesis started from the corresponding 1-tetralones **3***a–f*, prepared by standard procedures. Introduction of the nitrogen atom at the C(2) position of the 1-tetralone system was carried out according to two alternative procedures (Scheme 2).

First, nitrosation of 1-tetralones **3***a,b,d–f* with butyl- or isoamyl nitrite in the presence of potassium *tert*-butoxide afforded the desired hydroxyiminotetralones **4***a,b,d–f* in 50–80% yield. The comparatively lower yields observed for **4***b*, *d*, and *f* can be explained as a consequence of the concomitant formation of benzoates **9***b,d,f* or **10**, resulting from alkoxide



1*a–i* **2***a–i*

	R	OH/N stereochemistry
a	H	*cis* or *trans*
b	5-OCH_3	*cis* or *trans*
c	5-OBzl	*trans*
d	6-OBzl	*trans*
e	7-OBzl	*trans*
f	5,8-$(OCH_3)_2$	*cis* or *trans*
g	5-OH	*trans*
h	6-OH	*trans*
i	7-OH	*trans*

SCHEME 1

[1]This work was presented in a preliminary form at the XX Reunión Bienal de la Real Sociedad Espanola de Química, Castellón, Spain, 1984.

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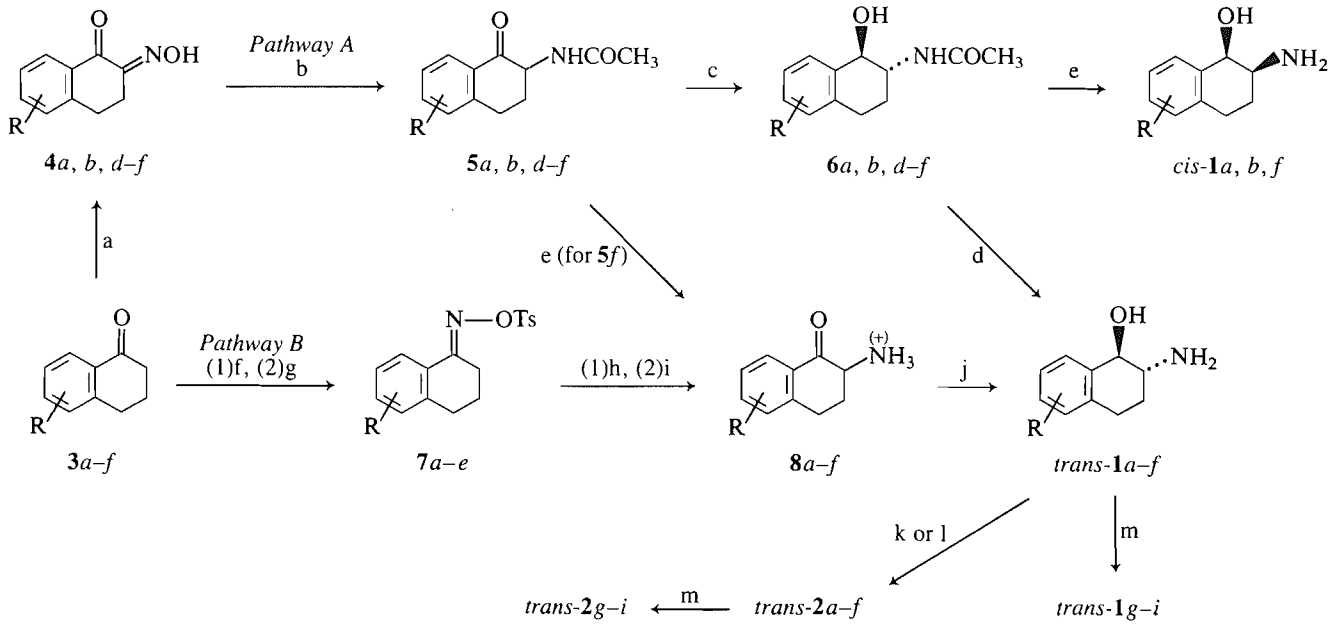
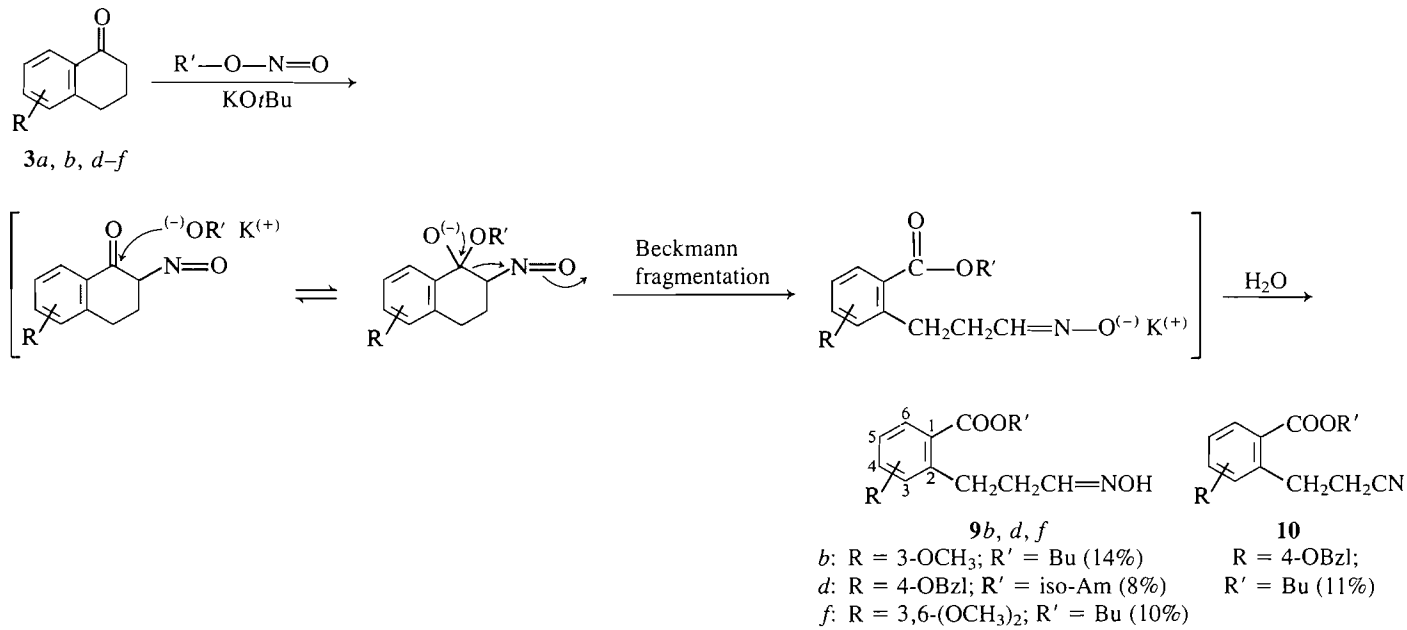
[3]Revision received November 10, 1987.



a: BuONO or iso-AmmONO/KO*t*-Bu; b: Zn, Ac_2O, AcOH; c: $NaBH_4$, CH_3OH, H_2O or H_2, PtO_2 (for **5f**); d: KOH, EtOH–H_2O; e: HCl 0.3 M rfx.; f: $NH_2OH \cdot HCl$, pyr.; g: Cl-OTs, pyr.; h: KOEt, benzene, EtOH (Neber rearrangement); i: HCl 5 M; j: $NaBH_4$, CH_3OH–NaOH; k: (1) acetone, benzene, rfx., (2) $NaBH_4$–CH_3OH; l: acetone, CH_3OH, $NaBH_3CN$; m: H_2, Pd/C 5%, 200 psi (from compounds *c*, *d*, and *e*).

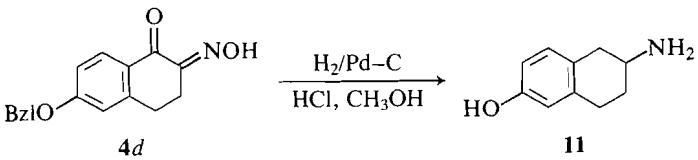
SCHEME 2



SCHEME 3

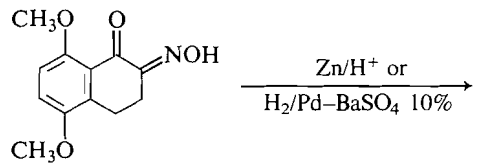
attack upon the C(1) position of the initially formed nitroso derivatives and subsequent Beckmann fragmentation (1) (Scheme 3). Nitrile **10** (arising from alkaline cleavage of the oximino ketone) (2) was obtained instead of the oxime, upon nitrosation of **3***d* with butyl nitrite. In general, short reaction times and low temperatures minimize or avoid the formation of the above fragmentation products.

Attempts to elaborate the 2-amino-1-tetralol moiety by direct reduction of hydroxyiminotetralones **4** were unsuccessful. Thus, hydrogenation of **4***d* over palladium–charcoal in acidic medium (3) afforded naphthylamine **11** as the only isolable product (Scheme 4). On the other hand, treatment of both **4***d* and **4***f* with lithium aluminum hydride (4) afforded only trace amounts of a *cis–trans* mixture of aminoalcohols **1***d* and **1***f*, respectively. In consequence, a stepwise reduction of oximino-tetralones **4***a*, *b*, *d–f* was envisaged. Thus, treatment of crude

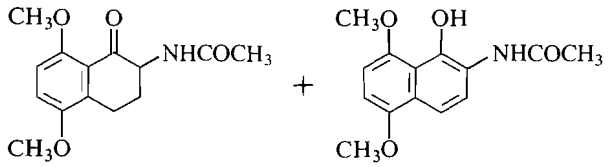


4*d* 11

SCHEME 4



4*f*



5*f* (55%) **12** (12%)

SCHEME 5

oximinotetralones with zinc dust in acetic acid – acetic anhydride solution (Scheme 2, pathway A), led to 2-acetamido-1-tetralones **5***a,b,d–f* in 55–65% yield. Reduction of **4***f* under the above conditions afforded a 5:1 mixture of **5***f* and naphthol **12** in 77% yield. Formation of **12** can be interpreted as a redox reaction between the hydroxyiminotetralone **4***f* and the initially formed acetamidotetralone **5***f* (Scheme 5). Alternative reduction of **4***f* by hydrogenation over Pd 10%/$BaSO_4$ in AcOH–Ac_2O (5) did not modify the above results.

Neber rearrangement (6) was used as the key step for the second (alternative) pathway to synthesize 2-amino-1-tetralols. The required tosyloxyderivatives **7***a–e* (Scheme 2, pathway B) were routinely obtained in two steps from the corresponding tetralones **3***a–e*. Neber rearrangement was not applied to the preparation of the 5,8-dimethoxylated aminoketone hydrochloride **8***f* since it is known that the steric hindrance exerted by the 8-OCH_3 group precludes formation of **7***f* from **3***f*-oxime (7). However, **8***f* could be obtained by acid hydrolysis of acetamidotetralone **5***f*.

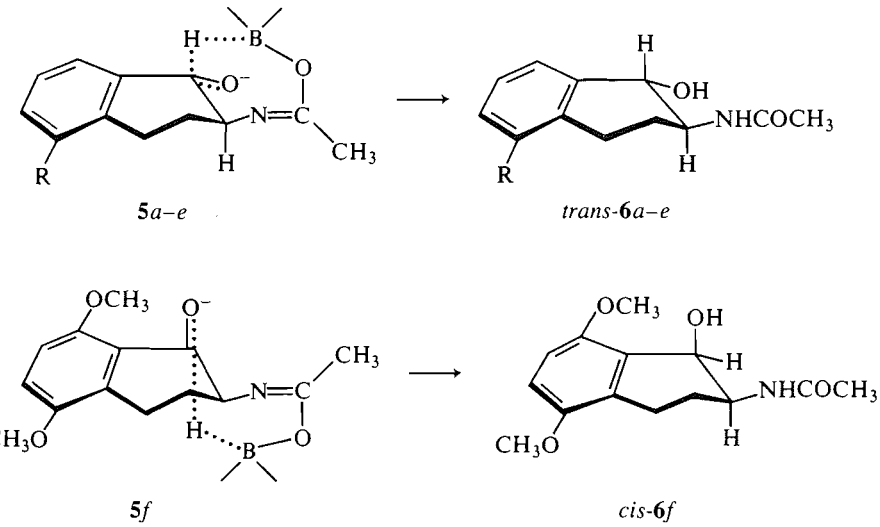
The stereoselective course of the reduction of the carbonyl group in 2-acetamido- and 2-amino-1-tetralones to give the corresponding *trans*-2-acetamido- or *trans*-2-amino-1-tetralols is well documented (5, 8, 9, 10). As expected, sodium borohydride reduction of compounds **5***a,b,d,e* in CH_3OH–H_2O (Scheme 2, pathway A) afforded the corresponding *trans* derivatives **6***a,b,d,e* as the major products (about a 90:10 *trans/cis* ratio based on C(1)H signal integration in the high resolution ^{1}H nmr spectra). The stereochemistry of compounds **6***a,b,d,e* was also confirmed by the $W_{1/2}$ value of about 16 Hz observed for the C(1)H proton, thus indicating a C(1)H–C(2)H pseudoaxial relationship. Alkaline hydrolysis of acetamidotetralols *trans*-**6***a,b,d,e* afforded the desired aminoalcohols *trans*-**1***a,b,d,e* in good yields, whose stereochemistry was confirmed by derivatization into conformationally restrained oxazolidin-2-one derivatives (11) as well as on the basis of the C(1)H chemical shift and coupling constant values (12, 13) of the cycloaliphatic protons (see below). On the other hand, aminoalcohols *trans*-**1***a–e* could be obtained by stereoselective sodium borohydride reduction of 2-amino-1-tetralone hydrochlorides **8***a–e* (again, about a 90:10 *trans/cis* ratio based on C(1)H signal integration was found).

The reverse stereoselectivity observed in the sodium borohydride reduction of the dimethoxylated derivatives **5***f* and **8***f* deserves comment. Thus, treatment under the above experimental conditions afforded in each case a mixture of diastereoisomers in which *cis* derivatives were predominant (about a 65:35 *cis/trans* ratio). Analysis of C(1)H signals in the high resolution ^{1}H nmr spectrum of the crude reaction mixture arising from sodium borohydride reduction of **5***f* revealed a doublet at 4.93 ppm (major isomer) whose coupling constant value (J = 4.3 Hz) was indicative of a *cis*-$OH_{axial}/NHR_{equatorial}$ relationship. Alkaline hydrolysis of this major isomer afforded aminoalcohol *cis*-**1***f*, whose stereochemistry was also confirmed on the basis of ^{1}H nmr data (see below). In the same way, sodium borohydride reduction of hydrochloride **8***f* afforded predominantly aminoalcohol *cis*-**1***f*. These results are opposite to those described by other authors (14), who assigned a *trans* stereochemistry to compound *cis*-**1***f*. The observed reversal of stereoselectivity can be rationalized according to House *et al.* (15, 16), assuming that the geometry of the transition state and that of the final product are similar and adequate to predict the major stereochemical course of borohydride reductions. Thus, the most stable transition state in the reduction of **5***a,b,d,e* and **8***a–e* would lead to a *trans*-OH/NHR diequatorial relationship, whereas the transition state leading to *cis*-**1***f* and *cis*-**6***f* from **5***f* and **8***f*, respectively, would be the most stable one, since steric crowding due to the "*peri*" effect between C(8) and C(1) groups is minimized. This interpretation does not preclude complexation between the 2-acetamido group and borane, which has been postulated in reduction of 2-amino-1-indanones (17).

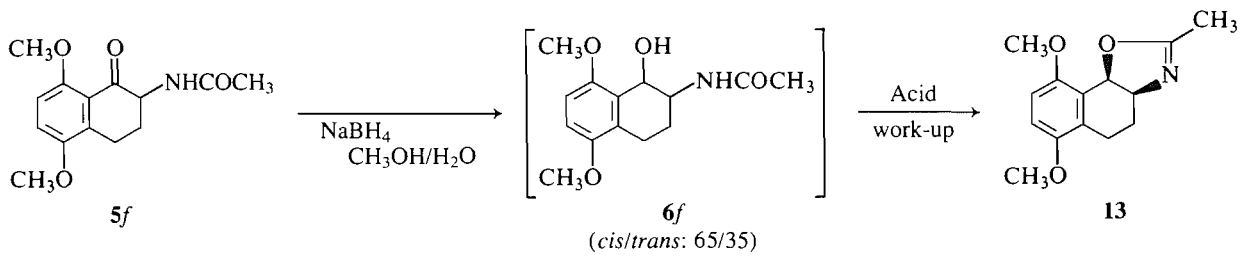
In contrast to borohydride reductions, hydrogenation over Adams catalyst of 2-acetamidotetralone **5***f* afforded predominantly *trans*-acetamidoalcohol **6***f* (about 80:20 *trans/cis* ratio based on ^{1}H nmr analysis), whose stereochemistry was confirmed by alkaline hydrolysis to aminoalcohol *trans*-**1***f*. The low coupling constant value (J = 4.9 Hz) between C(1)H–C(2)H for *trans*-**6***f* in $CDCl_3$ solution was indicative of the preferred OH/NHR *trans*-diaxial conformation in which *peri* interactions between C(1)H and C(8)OCH_3 groups are avoided. Likewise, the C(1) chemical shift observed for *trans*-**6***f* (see Table 3) is in agreement with the proposed OH-pseudoaxial disposition (18).

In summary, aminoalcohols *trans*-**1***a,b,d,e* could be obtained in comparable yields from the corresponding tetralones **3** by either of the two alternative pathways outlined in Scheme 2 (overall yields: pathway A, 18–20%; pathway B: 12–15%). Finally, hydrogenolysis of aminoalcohols *trans*-**1***c–e* over 5% palladium–charcoal (200 psi; 1 psi = 6.9 kPa) afforded the desired phenolic derivatives *trans*-**1***g–i* in about 50% yield. Attempts to carry out hydrogenolysis under atmospheric pressure gave only starting aminoalcohols whereas hydrogenation under acidic conditions resulted in simultaneous hydrogenolysis of benzyl and 1-hydroxyl groups.

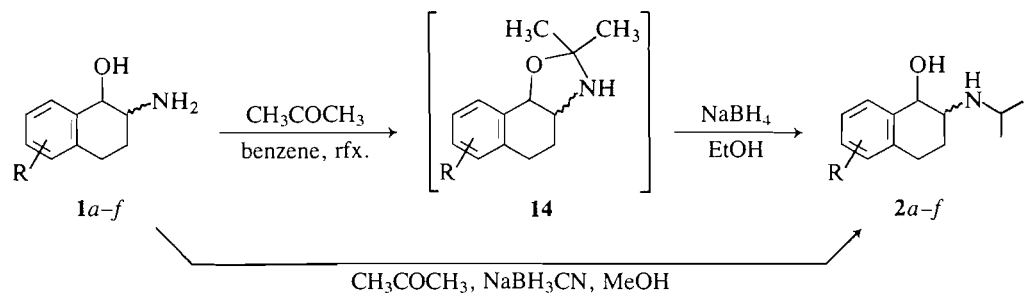
Aminoalcohols *cis*-**1***a*, *b*, and *f* could be readily obtained by acid hydrolysis of acetamidotetralols *trans*-**6***a,b*, and *f*, through a process that is known to proceed via an oxazoline intermediate with inversion of configuration at the C(1) carbon atom (10). Formation of the intermediate oxazoline was found to be very favourable upon acidic treatment of both *cis*- and *trans*-**6***f*. In fact, acidic work-up after sodium borohydride reduction of **5***f* afforded exclusively tetrahydronaphtho[2,1-*d*]oxazol derivative **13** (Scheme 7). Formation of



SCHEME 6



SCHEME 7



SCHEME 8

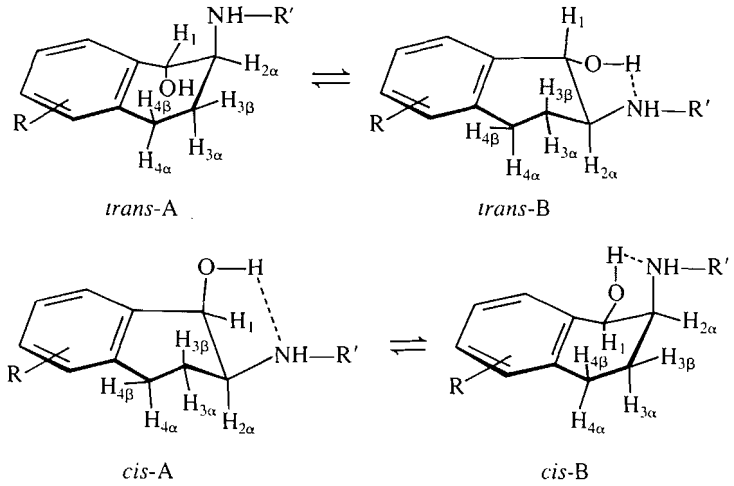
13 could be also carried out in an ^{1}H nmr tube. Thus, in the presence of a few drops of TFA, both *cis*- and *trans*-**6***f* in $CDCl_3$ gave an identical product whose ^{1}H nmr signals were superimposable on those of **13** recorded on $CDCl_3$ + TFA. On the other hand, alkaline hydrolysis of **13** afforded aminoalcohol *cis*-**1***f* as the only reaction product. The straightforward formation of **13** from *trans*-**6***f* can be explained in the light of the major *trans*-diaxial OH/NHR conformation of the starting 2-acetamidotetralol (see below).

Isopropyl derivatives **2** were obtained in each case from the corresponding *cis* or *trans* aminoalcohols either by reductive alkylation with excess acetone in benzene followed by sodium borohydride reduction of the intermediate oxazolidine system **14** (19) or in a one-step procedure with acetone – sodium cyanoborohydride in methanol (20) (Scheme 8). As in the amino series, isopropylamino derivatives *trans*-**2***g–i* were obtained by benzyl group hydrogenolysis as described above.

Conformational analysis

Although 2-aminotetrahydro-1-naphthols can be regarded as conformationally restrained analogues of adrenergic arylethanolamines, two limited half-chair conformations are still possible for each compound. Since interpretation of pharmacological data requires the knowledge of the preferred conformation in solution of the molecule under study, we have carried out a conformational analysis of the target aminotetrahydronaphthols by means of nmr data and theoretical calculations.

Assignment of the *cis* or *trans* OH/NHR relationship in amino or isopropylaminotetralols **1** and **2** can usually be carried out by simple inspection of ^{1}H nmr spectra, on the basis of C(1)H chemical shift and coupling constant differences in each diastereomer (12, 13). Thus, whereas compounds *cis*-**1***a,b,f* and *cis*-**2***a,b,f* showed a mean $\delta_{C(1)H}$ ($\pm$SD) of 4.68 ($\pm$0.16) ppm and a mean coupling constant J_{1-2} = 3.7 ($\pm$0.3) Hz, *trans* derivatives **1***a–i* and **2***a–i* (except for *trans*-**1***f* and *trans*-**2***f*, see



SCHEME 9

TABLE 1. Chemical shifts (ppm) and coupling constants (Hz) for *cis*-**1***b*, *trans*-**1***b*, and *trans*-**1***f* obtained from the LAOCOON/3 analysis*

Protons	*cis*-**1***b*†	*trans*-**1***b*†	*trans*-**1***f*†	*trans*-**1***f*‡
δH_1	4.55	4.30	4.68	4.63
δH_2	3.03	2.92	3.17	3.13
δH_3	1.84	2.00	2.07	2.06
δH_3	1.92	1.68	1.69	1.64
δH_4	2.57	2.79	2.67	2.64
δH_4	2.91	2.83	2.90	2.66
$J(H_1-H_{2\alpha})$	3.2	8.9	7.2	3.6
$J(H_{2\alpha}-H_{3\alpha})$	3.2	3.2	3.2	2.9
$J(H_{2\alpha}-H_{3\beta})$	10.4	11.3	10.8	5.5
$J(H_{3\alpha}-H_{4\alpha})$	6.8	11.9	5.3	7.0
$J(H_{3\alpha}-H_{4\beta})$	4.3	5.6	4.3	9.0
$J(H_{3\beta}-H_{4\alpha})$	10.1	5.9	10.4	4.6
$J(H_{3\beta}-H_{4\beta})$	5.9	3.6	5.3	5.6

*Intensity threshold in all cases was 0.05. The total number of transitions above the intensity threshold was 80, and 60–65 transitions were used in the fitting.
†$CDCl_3$ solution.
‡DMSO-d_6 solution.

below) showed average values of $\delta_{C(1)H} = 4.26$ (±0.13) ppm and $J_{1-2} = 8.6$ (±0.8) Hz. Finally, stereochemistry of 2-amino-1-tetralols has also been confirmed independently by derivatization into the corresponding tricyclic oxazolidin-2-one derivatives (11).

The cycloaliphatic region of the ^1H nmr spectra of *cis* derivatives **1***a*,*b*,*f* and **2***a*,*b*,*f* was almost superimposable. Consequently, we decided to carry out the spin system analysis by means of the LAOCOON-3 program of compound *cis*-**1***b*, which was taken as standard for this purpose (Table 1). Coupling constant values between C(2)H and $C(3)H_\alpha/C(3)H_\beta$ indicate a C(2)H axial disposition and, accordingly, a major or exclusive conformation in which the OH group is pseudoaxial and the NHR group is pseudoequatorial. In this conformation, *peri* interaction between the C(1)OH and C(8) groups (H in *cis*-**1***b*) is avoided and intramolecular OH–NHR hydrogen bonding can be established. Pseudoequatorial C(1)H disposition in *cis* derivatives was confirmed by a nuclear Overhauser effect (nOe) (21) enhancement. Thus, irradiation of the $C(8)OCH_3$ group of *cis*-**1***f* gave rise to a C(1)H nOe enhancement of 13%. On the other hand, a long-range *W* coupling (22) ($J = 0.9$ Hz) was also observed for C(1)H with C(3α)H in *cis*-**1***f* and *cis*-**2***f* derivatives, thus indicating a pseudoequatorial disposition for the above proton.

Theoretical calculations may be used as an independent criterion for performing conformational analysis. By means of the highly reliable Allinger's MM2 force field program (23), energies and geometries of both limited conformers *cis*-A and *cis*-B (Scheme 9) of compounds *cis*-**1***b* and *cis*-**1***f* have been calculated (Table 2). In both cases, *cis*-A conformers turned out to be more stable than the corresponding *cis*-B ones; the observed steric energy differences between them indicate a *cis*-A/*cis*-B relative population of 99:1, which is in agreement with the results of the ^1H nmr study. Moreover, application of the Karplus–Altona equation (24) to the dihedral angles obtained from MM2 analysis afforded a set of coupling constants (Table 2) very similar to those experimentally found (Table 1).

As in the *cis* series, *trans* derivatives **1***a–e* and **2***a–e* showed a nearly superimposable cycloaliphatic region in their ^1H nmr spectra. Spin system analysis of the model compound *trans*-**1***b* (Table 1) indicates a pseudoaxial C(2)H disposition and, consequently, a dipseudoequatorial relationship between amino and hydroxyl groups. This conformation is stabilized by intramolecular hydrogen bonding (broad signal between 3500 and 3000 cm^{-1} in the ir spectra), which overcomes the low *peri* interaction between C(1)OH and C(8)H groups. Accordingly, MM2 calculations for *trans*-A and *trans*-B conformers indicate the higher stability of the diequatorial *trans*-B conformer ($\Delta E =$ 1.21 kcal/mol) as well as a relative population of about 90:10 *trans*-B vs. *trans*-A. Once again, application of the Karplus–Altona equation to the predicted C(2)H coupling constants afforded mean *J* values in agreement with the experimental ones.

Dimethoxylated derivatives *trans*-**1***f* and *trans*-**2***f* were exceptional, since C(1)H protons showed lower J_{1-2} coupling constant and chemical shift values (0.3–0.4 ppm) with respect to C(8) unsubstituted derivatives, such as *trans*-**1***b* (Table 1). This is consistent with an equilibrium between *trans*-A and *trans*-B conformers in which participation of *trans*-A would be important to avoid the strong *peri* interaction between C(1)OH and $C(8)OCH_3$ groups. This situation stands out in DMSO-d_6

TABLE 2. Selected coupling constants, dihedral angles, and relative energies of *cis*-**1***b*, *trans*-**1***b*, *cis*-**1***f*, and *trans*-**1***f* (from MM2 analysis and the Karplus–Altona equation)

		Conformer A*			Conformer B*					
Compound	Protons	θ	*J* calcd.	Steric energy	θ	*J* calcd.	Steric energy	$\Delta E = E_A - E_B$ (kcal/mol)	% A/B	*J* average
	H_1–$H_{2\alpha}$	−49.08	3.06		45.30	4.69				3.08
cis-**1***b*	$H_{2\alpha}$–$H_{3\alpha}$	65.66	2.88	6.27	−60.25	2.59	8.97	−2.70	99/1	2.89
	$H_{2\alpha}$–$H_{3\beta}$	−174.43	11.82		59.29	3.73				11.73
	H_1–$H_{2\alpha}$	−49.99	2.96		35.75	5.82				2.97
cis-**1***f*	$H_{2\alpha}$–$H_{3\alpha}$	65.90	2.85	9.89	−60.11	2.61	13.51	−3.62	99/1	2.85
	$H_{2\alpha}$–$H_{3\beta}$	−174.02	11.81		59.74	3.66				11.79
	H_1–$H_{2\alpha}$	−74.45	1.96		−168.15	8.63				7.87
trans-**1***b*	$H_{2\alpha}$–$H_{3\alpha}$	−59.57	2.67	7.93	65.92	2.85	6.72	1.21	10/90	2.83
	$H_{2\alpha}$–$H_{3\beta}$	59.85	3.65		−174.07	11.81				10.88
	H_1–$H_{2\alpha}$	−74.00	2.01		−158.41	7.49				2.78
trans-**1***f*	$H_{2\alpha}$–$H_{3\alpha}$	−59.78	2.65	11.57	64.98	2.96	12.64	−1.07	85/15	2.69
	$H_{2\alpha}$–$H_{3\beta}$	59.80	3.66		−174.64	11.82				4.81

*See Scheme 9.

solution (J_{1-2} = 3.5 Hz for *trans*-**1***f*) more than in $CDCl_3$ solution (J_{1-2} = 7.2 Hz for *trans*-**1***f* and 6.2 Hz for *trans*-**2***f*), probably due to the solvating properties of DMSO, which stabilizes the *trans*-A conformation by intermolecular hydrogen bonding. As expected, intramolecular hydrogen bonding is reinforced by protonation of the amino group. Thus, the J_{1-2} value for *trans*-**1***f* in DMSO-d_6 + TFA rises to 6.4 Hz, which is in agreement with a major *trans*-B conformation as in *trans*-**1***a–e* derivatives. The major *trans*-A conformation of *trans*-**1***f* in DMSO-d_6 solution was confirmed by a C(1)H nOe enhancement of 10% on irradiation of the C(8)OCH_3 group. However, although these findings are indicative of conformational equilibrium, no variation of J_{1-2} coupling constants was observed in the temperature range between −60°C ($CDCl_3$) and +60°C (DMSO-d_6).

As above, results of MM2 force field calculations of *trans*-**1***f* (Table 2) were in agreement with ^{1}H nmr experimental data. Thus, the *trans*-A diaxial conformer turned out to be more stable than the *trans*-B (ΔE = 1.07 kcal/mol), and a relative population of about 85% could be estimated for the former. Coupling constant values derived from the Karplus–Altona equation (Table 2) correlate well with those found experimentally in DMSO-d_6 (Table 1). However, spin system analysis of *trans*-**1***f* in $CDCl_3$ afforded a set of coupling constants similar to those found for *trans*-**1***b* by MM2 calculations, which implies the predominance of the diequatorial *trans*-B conformation in nonpolar solvents.

Finally, ^{13}C nmr data (Table 3) are also in good agreement with the above results. Thus, in $CDCl_3$ solution, carbon atom C(1) is observed at 73.2 (±1.4) ppm in *trans* isomers and at 66.5 (±3.2) ppm in *cis* ones. The upfield shift found in *cis* isomers is consistent with the known shielding effect exerted by a pseudoaxial C(1)OH group upon the benzylic carbon atom in a tetralol system (18). On the other hand, carbon atom C(3) is also shielded in some *cis* isomers with respect to *trans* ones, due to a γ-*gauche* effect exerted by the pseudoaxial C(1)OH group. As expected, the C(1) chemical shift of *trans*-**1***f* in DMSO-d_6 solution showed an upfield shift of about 6 ppm, whereas C(3) and C(4) carbon atoms were shielded 3.8 and 2.9 ppm, respectively. Once again, this is consistent with the major *trans*-A diaxial conformation expected for *trans*-**1***f* in this solvent.

Experimental

Melting points were determined in a capillary tube on a Buchi apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 1430 spectrophotometer. Proton magnetic resonance spectra were measured at 60 MHz with a Perkin–Elmer R 24B instrument or at 200 MHz with a FT Varian XL-200 spectrometer. Signal positions are reported in ppm downfield from tetramethylsilane (δ scale) as an internal standard, and $CDCl_3$ as a solvent, unless otherwise indicated. The ^{13}C nmr spectra were measured at 50.3 MHz with a Varian XL-200 spectrometer, with internal tetramethylsilane as a reference. Multiplicity of the signal was determined by the ADEPT program (25). Homonuclear chemical shift correlation ^{1}H/^{1}H was determined by the HOMCOR program (26) and heteronuclear chemical shift correlation ^{13}C/^{1}H by the HETCOR program (27). MM2 calculations were performed on an IBM/3083 computer. Mass spectra were recorded on a Hewlett–Packard 5930 A spectrometer. Solutions in organic solvents were dried over anhydrous sodium sulfate and stripped of solvent with a rotary evaporator connected to a water aspirator. Microanalyses were performed by the Departamento de Quimica Organica Biologica (C.S.I.C.), Barcelona.

General synthetic methods

*Benzyl-3,4-dihydro-2*H*-1-naphthalenones (***3***c–e)*

Method A

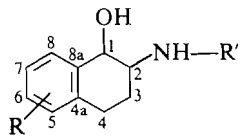
To a mixture of 0.1 mol of the corresponding hydroxytetralone **3***g* (28), **3***h* (29), or **3***i* (30) and 0.25 mol of anhydrous potassium carbonate, 0.1 mol of benzyl chloride in 150 mL of dry dimethylformamide was added dropwise. The reaction mixture was stirred at 80–100°C for 4 h, poured into ice-water and extracted with ether. The organic extracts were washed with brine, dried, and evaporated to afford **3***c–e*. Compound **3***c* (see also Table 4), ir ($CHCl_3$): 1680 (C=O); ^{1}H nmr (CCl_4): 2.0 (m, 2H, C(3)H_2), 2.4 (m, 2H, C(2)H_2), 2.8 (m, 2H, C(4)H_2), 4.9 (s, 2H, $CH_2C_6H_5$), 6.7–7.5 (m, 3H, ArH), 7.1 (s, 5H, C_6H_5). Compound **3***d* (see also Table 4), ir (KBr): 1660 (C=O), 1600; ^{1}H nmr (CCl_4): 2.0 (m, 2H, C(3)H_2), 2.4 (t, 2H, C(2)H_2), 2.7 (t, 2H, C(4)H_2), 4.8 (s, 2H, $OCH_2C_6H_5$), 6.5 (s, 1H, C(5)H), 6.6 (dd, 1H, C(7)H), 7.1 (s, 5H, C_6H_5), 7.6 (d, 1H, C(8)H). Compound **3***e* (10) (80%).

*2-Hydroxyimino-3,4-dihydro-2*H*-1-naphthalenones (***4***a,b,d–f)*

Method B

An ice-cooled solution of 30 mmol of potassium *tert*-butoxide,

TABLE 3. ^{13}C nuclear magnetic resonance data (tetrahydronaphthalene carbon atoms) of 2-amino-1,2,3,4-tetrahydro-1-naphthalenols ($CDCl_3$ solution)



Compound	R	R′	C(1)	C(2)	C(3)	C(4)	C(4a)	C(5)	C(6)	C(7)	C(8)	C(8a)
trans-**1***a*	H	H	74.8	53.8	29.1	27.7	135.6#	126.0*	126.9*	127.0*	128.1*	137.9#
cis-**1***a*	H	H	69.8	50.7	(28.0)	(27.5)	135.9#	126.2*	127.8*	128.6*	130.2*	137.2#
trans-**1***b*	5-OCH_3	H	74.7	53.4	28.5	22.0	124.6	156.5	108.2	126.6	118.8	139.4
cis-**1***b*	5-OCH_3	H	69.7	50.3	25.9	21.6	124.9	156.8	108.8	126.7	122.0	138.5
trans-**1***c*	5-OBzl	H	74.3	53.2	28.7	21.9	124.6	155.0	109.3	126.0	119.8	141.0
trans-**1***d*	6-OBzl	H	74.2	54.1	29.0	27.7	137.4	112.8*	157.0	113.4*	127.8	132.3
trans-**1***e*	7-OBzl	H	74.7	53.9	29.4	26.8	128.3	128.9	113.6*	156.7	113.4*	141.1
trans-**1***f*	5,8-$(OCH_3)_2$	H	72.6	52.6	27.4	21.5	127.2*	151.1#	(107.7)	(108.6)	152.0#	127.3*
cis-**1***f*	5,8-$(OCH_3)_2$	H	63.7	50.9	25.1	23.7	126.1*	151.8#	(108.1)	(109.0)	150.8#	128.8*
trans-**2***a*	H	i-Pr	73.2	57.9	28.3	26.8	138.0#	126.9*	127.0*	128.2*	126.2*	135.5#
cis-**2***a*	H	i-Pr	67.2	54.4	24.4	27.7	136.9#	126.2*	127.7*	128.5*	130.6*	135.9#
trans-**2***b*	5-OCH_3	i-Pr	72.4	56.9	25.3	21.9	124.5	156.4	108.2	126.6	119.1	139.2
cis-**2***b*	5-OCH_3	i-Pr	67.3	53.9	23.7	21.5	125.1	156.8	108.8	126.8	122.5	138.4
trans-**2***c*	5-OBzl	i-Pr	72.9	57.5	23.1	22.7	124.4	155.7	109.7	126.7	119.3	139.6
trans-**2***d*	6-OBzl	i-Pr	72.4	57.8	26.2	28.0	137.1	113.8*	157.7	113.1*	128.6	130.7
trans-**2***e*	7-OBzl	i-Pr	73.2	58.1	(27.5)	(27.1)	127.5	127.7	114.7*	157.4	112.1*	139.2
trans-**2***f*	5,8-$(OCH_3)_2$	i-Pr	69.7	55.6	22.7	21.0	128.4#	151.2*	(107.8)	(108.7)	152.3*	127.5#
cis-**2***f*	5,8-$(OCH_3)_2$	i-Pr	61.6	53.9	(23.4)	(23.6)	127.0#	151.3*	(107.7)	(109.3)	152.6*	127.3#

Parentheses and the superscripts * and # imply that the values may be interchanged.

in 35 mL of *tert*-butanol and 150 mL of dry ether under a nitrogen atmosphere, was treated with 28 mmol of the appropriate tetralone **3***a*–*f* and 36.5 mmol of freshly distilled butyl nitrite or isoamyl nitrite. After heating at reflux temperature (3 h for tetralones **3***a*, **3***c*, and **3***d*, and 10 min for tetralone **3***e*) or stirring at room temperature for 30 min (tetralones **3***b* and **3***f*) the reaction mixture was quenched with water and washed with ether. The aqueous phase was made acidic with 2 *M* HCl and extracted with dichloromethane to afford hydroxyiminotetralones. Compounds **4***a* (5) (85%), **4***b* (66%), and **4***f* (52%) were used without further purification. Compound **4***b*, ir (KBr): 3300–3100 (OH), 1720 (C=O), 1580 (C=N); ^1H nmr: 2.9 (m, 4H, $C(3)H_2$ + $C(4)H_2$), 3.8 (s, 3H, OCH_3), 6.6–7.7 (m, 3H, arom.). Compound **4***d* (*E* isomer) (see also Table 4), ir (KBr): 3500–3000 (OH), 1680 (C=O), 1590 (C=N); ^1H nmr (DMSO-d_6): 2.9 (s, 4H, $C(3)H_2$ + $C(4)H_2$), 4.9 (s, 2H, $OCH_2C_6H_5$), 6.6 (s, 1H, C(5)H), 6.7 (dd, J = 8 Hz and J = 2 Hz, 1H, C(7)H), 7.1 (s, 5H, C_6H_5), 7.7 (d, J = 8 Hz, 1H, C(8)H); ms, *m/e* (relative intensity): 281 (0.2), 91 (100). Compound **4***e*, (10) (60%). Compound **4***f*, ir (KBr): 3200 (OH), 1695 (C=O); ^1H nmr: 2.9 (s, 4H, $C(3)H_2$ + $C(4)H_2$), 3.7 (s, 3H, OCH_3), 6.7 (s, 2H, arom.), 7.8 (br, 1H, =N—OH).

Evaporation of the ethereal washings from reaction of tetralone **3***d* with isoamyl nitrite afforded a residue, which was chromatographed on silica gel. On elution with benzene – ethyl acetate (95:5), the *Z* isomer of oxime **4***d* was isolated (Table 4); ir ($CHCl_3$): 2900–2800 (OH str), 1600 (N=O); ^1H nmr: 2.9 (s, 4H, $C(3)H_2$ + $C(4)H_2$), 4.9 (s, 2H, $OCH_2C_6H_5$), 6.6 (s, 1H, C(5)H), 6.8 (dd, J = 9 Hz and J = 2 Hz, 1H, C(7)H), 7.2 (s, 5H, C_6H_5), 7.8 (d, J = 9 Hz, 1H, C(8)H), 15.2 (s, 1H, =NOH); ms, *m/e* (relative intensity): 281 (0.2), 91 (100). On elution with benzene – ethyl acetate (90:10), a mixture of *E*- and *Z*-4-benzyloxy-2-(2-formylethyl)isopentyl benzoate oximes (**9***d*) was isolated (Table 4); ir (NaCl): 3500–3150 (N—OH), 1710 (C=O), 1610 (C=N); ^1H nmr: 0.9 (d, 6H, CH_3-ipr), 1.5 (m, 3H, CH_2CH), 2.5 (m, 2H, CH_2CH=N), 3.1 (m, 2H, CH_2Ar), 4.1 (m, 2H, $COOCH_2$), 4.9 (s, 2H, $CH_2C_6H_5$), 6.6 (m, 1H, CH=N), 6.6 (s, 1H, C(5)H), 7.2 (s, 5H, C_6H_5), 7.2 (m, 1H, C(7)H), 7.8 (d, 1H, C(8)H), 8.3 (br, 1H, N—OH); ms, *m/e* (relative intensity): 369 (0.05), 91 (100).

Ethereal washings from reaction of tetralone **3***d* with butyl nitrite afforded a residue, which was chromatographed on silica gel. On elution with benzene – ethyl acetate (90:10), butyl 4-benzyloxy-2-(2-cyanoethyl)benzoate **10** (Table 4) was obtained; ir (NaCl): 2240 (CN), 1710 (C=O); ^1H nmr (CCl_4): 0.9 (m, 3H, CH_3), 1.1–1.8 (m, 4H, $CH_2CH_2CH_3$), 2.5 (t, 2H, CH_2CN), 3.1 (t, 2H, CH_2Ar), 4.1 (t, 2H, $COOCH_2$), 4.9 (s, 2H, $OCH_2C_6H_5$), 6.6 (dd, 1H, C(7)H), 6.7 (s, 1H, C(5)H), 7.1 (s, 5H, C_6H_5), 7.7 (d, 1H, C(8)H); ms, *m/e* (relative intensity): 337 (1), 105 (20), 91 (100).

Similarly, ethereal washings from reaction of tetralones **3***b* and **3***f* with butyl nitrite afforded oximes **9***b* and **9***f*, respectively (Table 4). Compound **9***b*, ir (KBr): 3300–3100 (OH), 1720 (C=O), 1580 (C=N); ^1H nmr: 0.8–1.9 (m, 7H, $CH_2CH_2CH_3$), 2.5 (m, 2H, CH_2=CH), 3.1 (m, 2H, $ArCH_2$), 3.7 (s, 3H, OCH_3), 4.2 (m, 2H, $COOCH_2$-), 6.5–7.5 (m, 4H, CH=N + 3H arom.), 8.3 (br, 1H, OH). Compound **9***f*, ir ($CHCl_3$): 3550, 3300, 1725, 1610; ^1H nmr: 0.7–1.9 (m, 7H, $CH_2CH_2CH_3$), 2.2–3.0 (m, 4H, $ArCH_2CH_2$), 3.6 (s, 6H, $2OCH_3$), 4.2 (t, 2H, $COOCH_2$), 6.6 (s, 2H, arom.), 7.2 (m, 1H, CH=N), 8.3–9.3 (br, 1H, =NOH); ms, *m/e* (relative intensity): 309 (13), 236 (24), 218 (50), 193 (100).

*2-Acetamido-3,4-dihydro-2*H*-naphthalenones (***5***a,b,d–f) Method C*

Zinc dust (190 mmol) was added portionwise to an externally cooled solution of 2-hydroxyiminotetralone (65 mmol) in 110 mL of acetic anhydride and 150 mL of acetic acid. After stirring for 1 h at room temperature, solids were removed by filtration and the solution was evaporated *in vacuo*. The residue was made alkaline with 2 *M* sodium hydroxide solution and extracted with dichloromethane. Evaporation of the organic phase afforded crude acetamidotetralones **5**. Acetamidotetralones **5***a* (5) (65%) and **5***b* (31) (62%) afforded analytical data comparable to those described in the literature. Compound **5***d* (see also Table 4), ir (KBr): 3320 (NH amide), 1680 (C=O), 1645–1620 (CONH); ^1H nmr: 1.3–2.0 (m, 1H, $C(3)H_e$), 2.0 (s, 3H, CH_3), 2.4–3.2 (m, 3H, $C(3)H_a$ + $C(4)H_2$), 4.2–4.7 (m, 1H, C(2)H), 5.0 (s, 2H, $OCH_2C_6H_5$), 6.4–6.8 (dd, 1H, C(5)H), 6.5 (s, 1H, NHCO), 6.5 (s, 1H, C(7)H), 7.1 (s, 5H, C_6H_5), 7.7 (d, 1H, C(8)H). Compound

TABLE 4. Elemental analyses and melting points

Compound	Molecular formula	Calculated				Found				Yield (%) (method)	Melting point (°C)	Crystallization solvents
		C	H	N	X*	C	H	N	X*			
cis-**1***a*	$C_{10}H_{13}NO\cdot(C_2H_2O_4)$	56.91	5.97	5.53	—	57.15	6.19	5.71	—	60(J)	163–165 (lit. (35) 213, HCl)	Ethanol
trans-**1***b*	$C_{11}H_{15}NO_2\cdot HCl$	57.52	7.02	6.09	15.43	57.55	7.21	6.02	15.61	45(H)/43(I)	224–226	Ethanol–ether
cis-**1***b*	$C_{11}H_{15}NO_2\cdot HCl$	57.52	7.02	6.09	15.43	57.59	7.30	6.18	15.61	61(J)	238–240	Ethanol–ether
trans-**1***c*	$C_{17}H_{19}NO_2\cdot HCl$	66.77	6.59	4.58	11.59	66.79	6.57	4.61	11.70	91(I)	245–247 (lit. (14) 139–141, base)	Ethanol–ether
trans-**1***d*	$C_{17}H_{19}NO_2\cdot\frac{1}{4}H_2O$	74.56	7.18	5.11	—	74.34	7.35	5.05	—	60(H)/75(I)	97–98 (lit. (32) 210–212, HCl)	Ether–hexane
trans-**1***e*	$C_{17}H_{19}NO_2\cdot\frac{1}{2}H_2O$	73.35	7.24	5.03	—	73.33	7.17	4.88	—	80(H)/90(I)	115–118 (lit. (10) 125–126)	Ether – ethyl acetate
trans-**1***f*	$C_{12}H_{17}NO_3\cdot HCl$	55.49	6.98	5.39	13.65	55.34	6.98	5.36	13.72	80(H)	195–196†	Ethanol–ether
cis-**1***f*	$C_{12}H_{17}NO_3\cdot HCl$	55.49	6.98	5.39	13.65	55.32	6.97	5.38	13.62	57(J)/71(H)	220–221†	Ethanol–ether
trans-**1***g*	$C_{10}H_{13}NO_2\cdot HCl$	55.69	6.54	6.49	16.44	55.68	6.55	6.54	16.21	85(M)	234–236	Ethanol–ether
trans-**1***h*	$C_{10}H_{13}NO_2$	67.02	7.31	7.81	—	67.05	7.40	7.50	—	46(M)	187–189	Methanol
trans-**1***i*	$C_{10}H_{13}NO_2$	67.02	7.31	7.81	—	67.09	7.61	7.77	—	50(M)	183–185 (lit. (10) 196–198)	Ethanol–ether
trans-**2***a*	$C_{15}H_{23}NO_3\cdot HCl$	59.69	8.01	4.64	11.74	59.69	8.11	4.64	11.82	75(L)	217–219	Ethanol–ether
cis-**2***a*	$C_{15}H_{23}NO_3\cdot HCl$	59.69	8.01	4.64	11.74	59.39	8.07	4.60	11.74	68(L)	204–205	Ethanol–ether
trans-**2***b*	$C_{14}H_{21}NO_2\cdot HCl$	61.87	8.16	5.15	13.04	61.59	8.15	5.06	13.21	98(K)	190–193	Ethanol–ether
cis-**2***b*	$C_{14}H_{21}NO_2\cdot HCl$	61.87	8.16	5.15	13.04	61.62	8.05	5.21	13.16	98(K)	255–256	Ethanol–ether
trans-**2***c*	$C_{20}H_{25}NO_2\cdot HCl$	69.05	7.53	4.02	10.19	68.88	7.83	3.90	10.20	91(K)	203–204 (lit. (14) 220–223)	Ethanol–ether
trans-**2***e*	$C_{20}H_{25}NO_2\cdot HCl$	69.05	7.53	4.02	10.19	68.81	7.70	3.97	10.22	85(K)	185–187	Ethanol–ether
trans-**2***f*	$C_{15}H_{23}NO_3\cdot HCl$	59.69	8.01	4.64	11.74	59.79	7.98	4.63	11.61	75(L)	217–219	Ethanol–ether
cis-**2***f*	$C_{15}H_{23}NO_3\cdot HCl$	59.69	8.01	4.64	11.74	59.39	8.07	4.60	11.74	68(L)	203–204	Ethanol–ether
trans-**2***g*	$C_{13}H_{19}NO_2\cdot HCl$	60.57	7.82	5.43	13.75	60.81	8.16	5.71	13.64	85(M)	Oil	(Chromatography)
trans-**2***i*	$C_{13}H_{19}NO_2\cdot HCl$	60.57	7.82	5.43	13.75	60.60	7.90	5.40	13.47	91(M)	195–197	Ethanol–ether
3*d*	$C_{17}H_6O_2$	80.92	6.39	—	—	81.05	6.51	—	—	78(A)	95–96	Hexane
3*e*-oxime	$C_{17}H_{17}NO_2$	73.68	6.41	5.24	—	76.49	6.52	5.26	—	89(E)	103–106	Ether–hexane
E-**4***d*	$C_{17}H_{15}NO_3$	72.58	5.37	4.98	—	72.41	5.33	4.90	—	58(B)	172 (dec.)	Ethyl acetate
Z-**4***d*	$C_{17}H_{15}NO_3$	72.58	5.37	4.98	—	72.35	5.21	4.96	—	3(B)	115–117	Ether
5*d*	$C_{19}H_{19}NO_3$	73.76	6.19	4.52	—	73.77	6.19	4.56	—	65(C)	156–158	Ether
5*f*	$C_{14}H_{17}NO_4$	63.86	6.50	5.32	—	63.59	6.50	5.32	—	55(C)	175–176	Ethyl acetate
trans-**6***d*	$C_{19}H_{21}NO_3$	73.29	6.80	4.50	—	73.29	6.83	4.53	—	70(D)	175–177	Methanol–ether
trans-**6***f*	$C_{14}H_{19}NO_4$	63.38	7.21	5.28	—	63.17	7.23	5.22	—	94	191–192	Ethyl acetate
cis-**6***f*	$C_{14}H_{19}NO_4$	63.38	7.21	5.28	—	63.34	7.47	5.18	—	51	137–138	Ether – ethyl acetate
7*b*	$C_{17}H_{19}NO_4S$	59.10	5.54	4.05	9.28	59.23	5.60	4.02	9.10	77(F)	150–152	Acetone
7*e*	$C_{24}H_{23}NO_4S\cdot\frac{1}{2}H_2O$	66.95	5.61	3.25	7.44	67.07	5.51	3.28	7.21	85(F)	112–115	Ether–acetone
8*b*	$C_{11}H_{13}NO_2\cdot HCl$	58.02	6.19	6.15	15.57	58.17	6.44	5.94	15.63	54(G)	210–212	Ethanol–ether
9*b*	$C_{15}H_{21}NO_4$	64.49	7.57	5.01	—	64.77	7.68	5.16	—	14(B)	84–85	Ether–hexane
9*d*	$C_{22}H_{27}NO_4$	71.52	7.36	3.79	—	71.71	7.44	3.78	—	8(B)	59–61	Ether–hexane
9*f*	$C_{16}H_{23}NO_5$	62.12	7.48	4.52	—	62.04	7.52	4.46	—	10(B)	64–66	Ether–hexane
12	$C_{14}H_{15}NO_4$	64.36	5.78	5.36	—	64.58	5.90	5.32	—	12(C)	130–131	Ether – ethyl acetate
13	$C_{14}H_{17}NO_3$	67.99	6.92	5.66	—	68.12	7.15	5.84	—	70	102–103	Ether–hexane

*Cl or S according to the formula.
†Literature (7) mp 199–202°C, mixture of *cis*-**1***f* and *trans*-**1***f* hydrochlorides.

5*e* (10) (60%). Compound **5***f* (see also Table 4), ir (KBr): 3300, 3100, 1705, 1670, 1640; ^{1}H nmr: 2.0 (s, 3H, CH_3CO), 2.6–3.3 (m, 4H, C(3)H_2 + C(4)H_2), 3.73 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.6 (m, 1H, C(2)H), 6.8 (dd, 3H, C(6)H + C(7)H + NHCO).

Reduction of acetamidotetralone **5***f* also afforded 2-acetamido-5,8-dimethoxy-1-naphthol **12** (Table 4) after chromatography of the crude reaction mixture (elution system: hexane – ethyl acetate 1:1); ir (KBr): 3430, 3340, 2850, 1690, 1530; ^{1}H nmr (200 MHz): 2.23 (s, 3H, CH_3CO), 3.91 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.57 (dd, 2H, C(6)H + C(7)H), 7.71 (d, J = 8 Hz, 1H, C(3)H), 7.84 (br, 1H, NHCO), 8.51 (d, J = 8 Hz, 1H, C(4)H), 9.69 (s, 1H, OH); ^{13}C nmr ($CDCl_3$): 28.4 (CH_3), 101.7, 103.7 (C-6 or C-7), 113.6 (C-3), 115.0 (C-4a), 120.1 (C-4), 122.8 (C-8a), 124.2 (C-2), 141.0 (C-1), 149.3, 150.3 (C-5 and C-8), 168.2 (CO).

trans-*2-Acetamido-1,2,3,4-tetrahydro-1-naphthalenols* (trans-**6**a,b,d,e) *Method D*

A solution of 285 mg (75 mmol) of sodium borohydride in 4 mL of water was added dropwise with external cooling to a solution of 15 mmol of the corresponding acetamidotetralone **5** in 15 mL of methanol. After stirring at room temperature until formation of a white precipitate, the resulting solid was washed with water and dried to afford *trans*-**6***a* (5) (80%), *trans*-**6***b* (31) (82%), *trans*-**6***d* (Table 4), and *trans*-**6***e* (10) (95%). Compound *trans*-**6***d*, ir (KBr): 3400–3100 (OH, NHCO), 1630; ^{1}H nmr (DMSO-d_6): 1.7 (s, 3H, CH_3CO), 1.8 (m, 2H, C(3)H_2), 2.7 (m, 2H, C(4)H_2), 3.4–4.0 (m, 2H, C(2)H), 4.3 (m, 1H, C(1)H), 4.9 (s, 2H, $OCH_2C_6H_5$), 6.5 (s, 1H, C(5)H), 6.7 (dd, 1H, C(7)H), 7.2 (d, 1H, C(8)H), 7.3 (s, 5H, C_6H_5), 7.6 (d, 1H, NH).

trans-*2-Acetamido-5,8-dimethoxy-1,2,3,4-tetrahydro-1-naphthalenol* (trans-**6**f)

A solution of 2.0 g (7.6 mmol) of acetamidotetralone **5***f* in 125 mL of methanol was hydrogenated (1 atm, 25°C) over 153 mg (0.78 mmol) of Adams catalyst. After absorption of the theoretical volume, the solution was filtered and the solvent was removed to afford a mixture of diastereomeric acetamidotetralols **6***f* (*trans*/*cis* ratio 9:1, based on ^{1}H nmr). Successive crystallizations afforded pure *trans*-**6***f* (Table 4), ir (KBr): 3350, 2950, 1660, 1540; ^{1}H nmr (200 MHz): 1.80 (m, 1H, C(3)H_a), 1.93 (s, 3H, CH_3CO), 2.16 (m, 1H, C(3)H_a), 2.76 (m, 2H, C(4)H_a + C(4)H_e), 3.78 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.20 (m, 1H, C(2)H), 4.84 (d, J = 4.97 Hz, 1H, C(1)H), 6.74 (s, 2H, C(6–7)H); ^{13}C nmr ($CDCl_3$): 20.0 (C-4), 22.7 (CH_3 and C-3), 50.7 (C-2), 66.1 (C-1), 108.6, 109.9 (C-6 and C-7), 126.2, 127.4 (C-4a and C-8a), 151.6, 153.1 (C-5 and C-8), 172.2 (CO).

cis-*2-Acetamido-5,8-dimethoxy-1,2,3,4-tetrahydro-1-naphthalenol* (cis-**6**f)

To an ice-cooled stirred suspension of 2.0 g (7.6 mmol) of 2-acetamidotetralone **5***f* in 20 mL of methanol, a solution of 144 mg (3.8 mmol) of sodium borohydride in 4 mL of water was added dropwise. After 1 h stirring at room temperature the reaction mixture was poured into 100 mL of water, and the methanol was removed *in vacuo*. The aqueous phase was extracted with dichloromethane and the organic extracts afforded a residue, which was chromatographed on silica gel. On elution with ethyl acetate, 1.4 g of a *cis–trans* mixture of acetamidotetralols **6***f* were obtained (*cis*/*trans* ratio, 65:35 based on ^{1}H nmr). Analytically pure *cis*-**6***f* was obtained by crystallization (Table 4); ir (KBr): 3350, 2950, 1640; ^{1}H nmr (200 MHz): 1.9 (m, C(3)H_{a+e}), 2.01 (s, 3H, CH_3CO), 2.58 (m, 1H, C(4)H_a), 2.95 (m, 1H, C(4)H_e), 3.78 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.02 (m, 1H, C(2)H), 4.93 (d, J = 4.25 Hz, 1H, C(1)H), 6.74 (m, 2H, C(6–7)H); ^{13}C nmr ($CDCl_3$): 22.7, 23.2 (C-3 and C-4), 23.5 (CH_3), 48.9 (C-2), 63.2 (C-1), 107.7, 109.5 (C-6 and C-7), 126.8, 127.0 (C-4a and C-8a), 151.4, 151.7 (C-5 and C-8), 169.6 (CO).

When the above reaction mixture was poured into 6 *M* hydrochloric acid, and the methanol was removed *in vacuo* on a steam-bath, similar work-up afforded *cis*-2-methyl-6,9-dimethoxy-3a,4,5,9b-tetrahydronaphtho[2,1-*d*]oxazol (**13**) (Table 4); ^{1}H nmr (200 MHz): 1.84 (m, 1H, C(3)H_a), 1.96 (s, 3H, CH_3), 2.10 (m, 1H, C(3)H_e), 2.48 (m, 1H, C(4)H_a), 2.89 (m, 1H, C(4)H_e), 3.84 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.48 (m, 1H, C(3)H_a), 5.87 (d, J = 9.7 Hz, 1H, C(9b)H), 6.74 (d, J = 8.9 Hz, 1H, arom.), 6.83 (d, J = 8.9 Hz, 1H, arom.); ms, *m*/*e* (relative intensity): 248 (6), 247 (30), 188 (100), 173 (96); ^{13}C nmr ($CDCl_3$): 14.1 (CH_3), 17.5 (C-5), 27.4 (C-4), 63.2 (C-3a), 73.3 (C-9b), 108.3, 110.0 (C-7 and C-8), 122.4 (C-5a), 130.4 (C-9a), 150.4, 152.8 (C-5 and C-8), 165.7 (C-2).

*3,4-Dihydro-2*H*-1-naphthalenone oximes* (**3**a–e *oximes*) *Method E*

A solution of 50 mmol of tetralone **3***a–e* and 8.0 g (115 mmol) of hydroxylamine hydrochloride in 25 mL of dry pyridine was heated at reflux temperature for 12 h. After pouring into water, the reaction mixture was extracted with dichloromethane and the organic layers were washed with 1 *M* hydrochloric acid and 0.5 *M* sodium bicarbonate. Evaporation of the organic solvent afforded the required oximes; **3***a*-oxime (33) (96%), **3***b*-oxime (34) (84%), **3***c*-oxime (14) (97%), **3***d*-oxime (32) (97%), and **3***e*-oxime (Table 4); ir (KBr): 3340–3000 (OH), 1620 (C=N); ^{1}H nmr: 1.4–1.9 (m, 2H, C(3)H_2), 2.4–2.8 (m, 4H, C(2)H_2 + C(4)H_2), 4.8 (s, 2H, $OCH_2C_6H_5$), 6.6–7.5 (m, C(5) + C(6) + C(8)), 7.2 (s, 5H, C_6H_5), 9.3 (br, 1H, N—OH).

*3,4-Dihydro-2*H*-1-naphthalenone* O*-tosyloximes* (**7**a–e) *Method F*

A solution of 43 g (75 mmol) of *p*-toluenesulfonyl chloride in 80 mL of dry pyridine was added dropwise to an ice-cooled solution of the requisite naphthalenone **6***a–e* oxime (75 mmol) in 80 mL of dry pyridine. After stirring for 16 h at room temperature, the reaction mixture was poured into water and extracted with dichloromethane. The organic layers were washed with 2 *M* hydrochloric acid, 0.5 *M* sodium bicarbonate, and dried. Evaporation afforded crude tosyloximes **7***a* (5) (83%), **7***c* (14) (90%), **7***d* (32) (89%), **7***b*, and **7***e* (Table 4). Compound **7***b*, ir (KBr): 1600, 1575; ^{1}H nmr: 1.5–2.0 (m, 2H, C(3)H_2), 2.4 (s, 3H, CH_3-Ar), 2.5–2.7 (m, 4H, C(2)H_2 + C(4)H_2), 3.7 (s, 3H, OCH_3), 6.6–7.4 (m, 3H, C(6–8)H), 7.2 (d, J = 8 Hz, 2H, C(3′)H + C(5′)H), 7.8 (d, J = 8 Hz, 2H, C(2′)H + C(6′)H). Compound **7***e*, ir (KBr): 1590; ^{1}H nmr: 1.7 (m, 2H, C(3)H_2), 2.3 (s, 3H, CH_3-Ar), 2.6 (m, 4H, C(2)H_2 + C(4)H_2), 4.9 (s, 2H, $OCH_2C_6H_5$), 6.7–7.3 (complex, 3H, C(5–8)H), 7.2 (s, 5H, C_6H_5), 7.4 (dd, 4H, C_6H_4—CH_3).

*2-Amino-3,4-dihydro-2*H*-1-naphthalenone hydrochlorides* (**8**a–e) *Method G*

To a stirred suspension of 16 mmol of tosyloxime **7***a–e* in 15 mL of dry benzene a solution of 16.5 mmol of potassium ethoxide in 10 mL of absolute ethanol was added at 0°C under a nitrogen atmosphere. After 24 h at room temperature, the reaction mixture was filtered and the filtrates were poured into 100 mL of 5 *M* hydrochloric acid. After 15 min stirring at room temperature, the aqueous phase was evaporated *in vacuo* (to afford crude hydrochlorides **8***a*,*b*) or the resulting precipitate was collected and dried (hydrochlorides **8***c–e*). In each case, crystallization from ethanol–ether afforded analytically pure samples. Compound **8***a* (33) (35%), **8***c* (14) (75%), **8***d* (32) (65%), **8***e* (10) (60%). Compound **8***b* (see also Table 4), ir (KBr): 3100, 2800, 1690–1640; ^{1}H nmr (D_2O): 2.1–3.3 (m, 4H, C(3)H_2 + C(4)H_2), 3.7 (s, 3H, OCH_3), 4.3 (dd, 1H, C(2)H), 7.2 (m, 3H, C(6–8)H).

*2-Amino-3,4-dihydro-5,8-dimethoxy-2*H*-1-naphthalenone hydrochloride* (**8**f)

A solution of 250 mg (0.95 mmol) of 2-acetamidotetralone **5***f* in 20 mL of 0.3 *M* hydrochloric acid was heated at reflux temperature. After 5 h, the reaction mixture was evaporated *in vacuo* to afford crude hydrochloride **8***f* (14), which was purified by crystallization from ethanol–ether 1:1 (overall yield, 75%).

trans-*2-Amino-1,2,3,4-tetrahydro-1-naphthalenols* (trans-**1**a–f) *Method H*

Alkaline hydrolysis of *trans*-**6***a*,*b*,*d–f*: To a solution of 7.5 mmol of the requisite acetamidotetralol *trans*-**6***a*,*b*,*d–f* in 80 mL of ethanol, a solution of 6.3 g (110 mg) of potassium hydroxide in 30 mL of water was added dropwise under nitrogen. After 12 h at reflux temperature, the reaction mixture was poured into water, and the ethanol was removed *in vacuo*. The residue was made acidic with 2 *M* hydrochloric acid and washed with ether. The aqueous layer was basified and

extracted with dichloromethane. The organic extracts were dried and evaporated to afford aminoalcohols *trans*-**1***a–f* (Table 4).

Method I

Sodium borohydride reduction of hydrochlorides **8***a–f*: Hydrochloride **8***a–f* (4 mmol) was added portionwise to an ice-cooled solution of sodium borohydride (200 mmol) in 5 *M* sodium hydroxide (4 mL) and methanol (40 mL). When the addition was complete, the reaction mixture was treated with another 20 mmol of sodium borohydride. After 15 min stirring, 100 mL of water were added, methanol was removed *in vacuo*, and the aqueous phase was extracted with dichloromethane. Evaporation of the aqueous layer afforded crude aminotetralols *trans*-**1***a–f*, which were purified by crystallization of the corresponding hydrochloride.

Compound *trans*-**1***a* (35) (Methods H and I, 45%), *trans*-**1***c* (14) (Method I, 91%), *trans*-**1***d* (32) (Method H, 75%; Method I, 60%). Compound *trans*-**1***b* (Table 4), ir (KBr): 3250, 1610, 1590; ^{1}H nmr (200 MHz, base, see also Table 1): 1.64 (m, 1H, C(3)H$_a$), 2.04 (m, 1H, C(3)H$_e$), 2.60 (m, 1H, C(4)H$_a$), 2.80 (m, 1H, C(4)H$_e$), 2.88 (m, 1H, C(2)H), 3.81 (s, 3H, OCH_3), 4.33 (d, J = 8.6 Hz, 1H, C(1)H), 6.72 (m, 1H, C(6)H), 7.18 (m, 2H, C(7–8)H); ^{13}C nmr: Table 3. Compound *trans*-**1***e* (Table 4), ir (KBr): 3310, 3250, 1610; ^{1}H nmr (200 MHz, base): 1.56–1.82 (m, 1H, C(3)H$_a$), 1.94–2.10 (m, 1H, C(3)H$_e$), 2.76–3.00 (m, 3H, C(4)H$_2$ + C(2)H), 3.10 (3H, exch.), 4.30 (d, J = 8.8 Hz, 1H, C(1)H), 5.06 (s, 2H, $OCH_2C_6H_5$), 6.82 (dd, J_o = 8.43 Hz, J_m = 2.72 Hz, 1H, C(6)H), 6.99 (d, J_o = 8.43 Hz, 1H, C(5)H), 7.19 (d, J_m = 2.72 Hz, 1H, C(8)H), 7.31–7.46 (m, 5H, C_6H_5); ^{13}C nmr: Table 3. Compound *trans*-**1***f* (Table 4), ir (KBr): 3400–3300, 2950, 1610; ^{1}H nmr (200 MHz, base, see also Table 1): 1.64 (m, 1H, C(3)H$_a$), 2.01 (m, 1H, C(3)H$_e$), 2.60 (m, 1H, C(4)H$_a$), 2.84 (m, 1H, C(4)H$_e$), 3.17 (m, 1H, C(2)H), 3.78 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.68 (d, J = 7.2 Hz, 1H, C(1)H), 6.70 (s, 2H, C(6–7)H); ^{13}C nmr ($CDCl_3$): Table 3; ^{13}C nmr (DMSO-d_6): 18.6 (C-4), 23.6 (C-3), 50.8 (C-2), 66.8 (C-1), 107.9, 108.6 (C-6 and C-7), 126.3, 127.1 (C-4a and C-8a), 150.5, 152.7 (C-5 and C-8).

cis-*2-Amino-1,2,3,4-tetrahydro-1-naphthalenols* (cis-**1**a,b,f)

Method J

A suspension of 650 mmol of acetamidotetralol *trans*-**6***a,b,f* in 15 mL of 0.3 *M* hydrochloric acid was heated under nitrogen at reflux temperature. After 5 h, the reaction mixture was washed with ether and the aqueous phase was evaporated *in vacuo*. The resulting crude hydrochloride was purified by crystallization from ethanol–ether. Compound *cis*-**1***a* (5) (60%). Compound *cis*-**1***b* (Table 4), ir (KBr): 3300, 1590, 1520; ^{1}H nmr (200 MHz, base, see also Table 1): 1.72–2.06 (m, 2H, C(3)H$_{a+e}$), 2.86 (m, 2H, C(4)H$_{a+e}$), 3.66 (m, 1H, C(2)H), 4.90 (d, J = 3.9 Hz, 1H, C(1)H), 7.30 (m, 5H, arom.); ^{13}C nmr: Table 3. Compound *cis*-**1***f* (Table 4), ir (KBr): 3330, 3280, 1600; ^{1}H nmr (200 MHz, base, see also Table 1): 1.82 (m, 2H, C(3)H$_{a+e}$), 2.50 (m, 1H, C(4)H$_a$), 2.92 (m, 2H, CH-iPr + C(2)H), 3.78 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.87 (d, J = 3.9 Hz, 1H, C(1)H), 6.70 (s, 2H, C(6)H + C(7)H); ^{13}C nmr: Table 3.

Alkaline hydrolysis of *cis*-**6***f* (Method H) also afforded aminoalcohol *cis*-**1***f* (Table 4). Alkaline hydrolysis of crude *cis*-**6***f* (*cis*/*trans* ratio 65:35) afforded a mixture of aminoalcohols *cis*-**1***f* and *trans*-**1***f*, which were separated by chromatography on neutral alumina (activity III) on elution with methanol.

2-Isopropylamino-1,2,3,4-tetrahydro-1-naphthalenols (**2**a–f)

Method K

To a suspension of 0.8 mmol of the corresponding 2-amino-1-tetralol in 7 mL of dry benzene, 4.5 mmol of anhydrous acetone was added. After 3 h stirring at reflux temperature, the solvent was removed *in vacuo*, the residue was dissolved in 5 mL of absolute ethanol, and sodium borohydride (2.1 mmol) was added portionwise to the above solution with external cooling. After 2 h stirring at room temperature, the reaction mixture was quenched with 2 *M* hydrochloric acid and the ethanol was removed *in vacuo*. The aqueous phase was washed with ether, made alkaline with 5 *M* sodium hydroxide, and extracted with dichloromethane. The organic extracts were dried and evaporated to afford isopropylamino derivatives *trans*-**2***c* (14) (85%), *trans*-**2***d* (32) (82%), *cis*-**2***b*, *trans*-**2***b*, and *trans*-**2***e* (Table 4). Compound *cis*-**2***b*, ir (KBr): 3250, 2890, 1560; ^{1}H nmr (200 MHz, base): 0.70 (d, 3H, CH_3CH), 1.10 (d, 3H, CH_3CH), 1.70 (m, 1H, C(3)H), 1.92 (m, 1H, C(3)H′), 2.60 (m, 1H, C(4)H$_a$), 2.86 (m, 1H, C(4)H$_e$), 3.04 (m, 2H, C(2)H + $CH(CH_3)_2$), 3.81 (s, 3H, OCH_3), 4.57 (d, J = 4.0 Hz, 1H, C(1)H), 6.76 (d, 1H, C(6)H), 7.08 (d, 1H, C(8)H), 7.18 (d, 1H, C(7)H); ^{13}C nmr: Table 3. Compound *trans*-**2***b*, ir (KBr): 3310, 2990, 1580; ^{1}H nmr (200 MHz, base): 0.98 (d, J = 6.2 Hz, 3H, CH_3CH), 1.05 (d, J = 6.2 Hz, 3H, CH_3CH), 1.46 (m, 2H, C(3)H$_{a+e}$), 2.12 (m, 1H, C(3)H$_a$), 2.68 (m, 3H, C(2)H + C(4)H$_2$), 2.96 (m, 1H, $CH(CH_3)_2$), 3.72 (s, 3H, OCH_3), 4.30 (d, J = 8.9 Hz, 1H, C(1)H), 6.64 (m, 1H, C(6)H), 7.12 (m, 2H, C(7–8)H); ^{13}C nmr: Table 3. Compound *trans*-**2***e*, ir (KBr): 3500–3100 (NH), 3100–2500 (OH); ^{1}H nmr (200 MHz, base): 1.06 (d, J = 6.1 Hz, 3H, CH_3CH), 1.13 (d, J = 6.1 Hz, 3H, CH_3CH), 1.49 (m, 1H, C(3)H$_a$), 1.65 (m, 1H, C(3)H$_e$), 2.20 (m, 1H, C(4)H$_a$), 2.71 (m, 1H, C(2)H), 2.83 (m, 3H, C(4)H$_e$ + exch.), 3.06 (m, 1H, CH—CH_3), 4.32 (d, J = 9.02 Hz, 1H, C(1)H), 5.06 (s, 2H, $OCH_2C_6H_5$), 6.83 (dd, J_o = 8.47 Hz, J_m = 2.79 Hz, 1H, C(6)H), 6.99 (d, J_o = 8.47 Hz, 1H, C(5)H), 7.22 (d, J_m = 2.79 Hz, 1H, C(8)H), 7.46 (m, 5H, C_6H_5); ^{13}C nmr: Table 3.

Method L

To a solution of 2-amino-1-tetralol (0.7 mmol) in 6 mL of methanol under nitrogen, sodium cyanoborohydride (3.5 mmol), acetone (3.5 mmol), and molecular sieve 3Å were added. After 18 h stirring at room temperature, the reaction mixture was poured into water and the methanol was removed *in vacuo*. The aqueous phase was made alkaline with 2 *M* sodium hydroxide and extracted with dichloromethane. The organic extracts were washed with water, dried, and evaporated to afford the corresponding isopropyl derivative (Table 4). Compound *cis*-**2***a*, ^{1}H nmr (200 MHz, base): 1.10 (d, 3H, CH_3CH), 1.14 (d, 3H, CH_3CH), 1.70 (m, 1H, C(3)H), 1.98 (m, 1H, C(3)H′), 2.84 (m, 2H, C(4)H$_2$), 3.06 (m, 2H, CH-iPr + C(2)H), 4.60 (d, J = 4.1 Hz, 1H, C(1)H), 7.30 (m, 5H, arom.); ^{13}C nmr: Table 3. Compound *trans*-**2***a*, ^{1}H nmr (200 MHz, base): 1.07 (d, J = 6.2 Hz, 3H, CH_3CH), 1.13 (d, J = 6.2 Hz, 3H, CH_3CH), 1.58 (m, 2H, C(3)H$_2$), 2.18 (m, 1H, C(4)H$_a$), 2.76 (m, 1H, C(2)H), 2.84 (m, 2H, C(4)H$_e$), 3.0 (m, 1H, CH-iPr), 4.37 (d, J = 9.1 Hz, 1H, C(1)H), 7.14 (m, 4H, C(5–8)H; ^{13}C nmr: Table 3. Compound *cis*-**2***f*, ^{1}H nmr (200 MHz, base): 1.09 (d, 3H, CH_3CH), 1.12 (d, 3H, CH_3CH), 1.74 (m, 2H, C(3)H$_{a+e}$), 2.50 (m, 1H, C(4)H$_a$), 2.84 (m, 1H, C(4)H$_e$), 2.92 (m, 1H, C(2)H), 3.09 (m, 1H, CH-iPr), 3.76 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.87 (d, J = 3.9 Hz, 1H, C(1)H), 6.71 (s, 2H, C(6–7)H; ^{13}C nmr: Table 3. Compound *trans*-**2***f*, ^{1}H nmr (200 MHz, base): 1.10 (t, 6H, CH-iPr), 1.61 (m, 1H, C(3)H$_a$), 2.04 (m, 1H, C(3)H$_e$), 2.67 (m, 2H, C(4)H$_{a+e}$), 3.05 (m, 2H, C(2)H + CH-iPr), 3.77 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.76 (d, J = 6.2 Hz, 1H, C(1)H), 6.69 (s, 2H, C(6–7)H); ^{13}C nmr: Table 3.

trans-*2-Amino-1,2,3,4-tetrahydronaphthalenediols* (trans-**1**g–i *and* trans-**2**g–i)

Method M

A solution of 3.5 mmol of the corresponding benzyloxy-2-amino-1-tetralol *trans*-**1***c–e* or *trans*-**2***c–e* in 100 mL of absolute methanol was hydrogenated in a Parr apparatus in the presence of 5% palladium on charcoal (350 mg) at 300 psi. After 24 h, the reaction mixture was filtered and the methanol was removed *in vacuo* to afford debenzylated aminotetralols **1***g–i* and **2***g–i* (Table 4). Compound *trans*-**1***g*, ^{1}H nmr (hydrochloride, D_2O, 200 MHz): 1.60 (m, 1H, C(3)H$_a$), 2.05 (m, 1H, C(3)H$_e$), 2.43 (m, 1H, C(4)H$_a$), 2.63 (m, 1H, C(4)H$_e$), 3.13 (m, 1H, C(2)H), 4.50 (d, J = 8.8 Hz, 1H, C(1)H), 6.59 (dd, J = 1.9 Hz, and J = 7.8 Hz, 1H, C(6)H or C(8)H), 6.84 (dd, J = 1.9 Hz, and J = 7.8 Hz, 1H, C(6)H or C(8)H), 6.96 (t, 1H, C(7)H). Compound *trans*-**2***g*, ^{1}H nmr (hydrochloride, D_2O, 200 MHz): 1.37 (d, J = 6.36 Hz, 3H, CH_3-iPr), 1.46 (d, J = 6.46 Hz, 3H, CH_3-iPr), 1.95 (m, 1H, C(3)H$_a$), 2.36 (m, 1H, C(3)H$_e$), 2.71 (m, 1H, C(4)H$_a$), 2.95 (m, 1H, C(4)H$_e$), 3.24 (dd, 1H, C(2)H), 3.58 (m, 1H, CH-iPr), 4.89 (d, J = 9.4 Hz, 1H, C(1)H), 6.73 (dd, 1H, C(7)H), 7.06–7.10 (m, 2H, C(6)H + C(8)H). Compound *trans*-**1***h* (10) (47%). Compound *trans*-**2***h* (32) (85%). Compound *trans*-**1***i*, ^{1}H nmr (base, 200 MHz): 1.65 (m, 1H, C(3)H$_a$), 1.99 (m, 1H, C(3)H$_e$), 2.80 (m, 3H, C(4)H$_2$ + C(2)H), 4.16 (br, 4H, exch.), 4.27 (d, J = 8.87 Hz, 1H, C(1)H), 6.67

(dd, J_o = 8.39 Hz, J_m = 2.57 Hz, 1H, C(6)H), 6.91 (d, J_o = 8.39 Hz, 1H, C(5)H), 6.96 (d, J_m = 2.57, 1H, C(8)H). Compound *trans*-**2***i* (hydrochloride, D_2O, 200 MHz): 1.17 (d, J = 6.5 Hz, 3H, CH_3-iPr), 1.22 (d, J = 6.5 Hz, 3H, CH_3-iPr), 1.28 (m, 1H, C(3)H_a), 1.65 (m, 1H, C(3)H_e), 2.19 (m, 2H, C(4)H_2), 2.72 (m, 1H, C(2)H), 3.03 (m, 1H, CH-iPr), 4.04 (d, J = 11.2 Hz, 1H, C(1)H), 6.64 (dd, J_o = 8.4 Hz, J_m = 2.6 Hz, 1H, C(6)H), 6.8 (d, J_m = 2.6 Hz, 1H, C(8)H), 6.92 (d, J_o = 8.4 Hz, 1H, C(5)H).

*6-Amino-5,6,7,8-tetrahydro-2-naphthalenol (**11**)*

A solution of 1.35 g (4.7 mmol) of hydroxyiminotetralone **4***d* in 50 mL of absolute methanol was hydrogenated (1 atm) in the presence of 5% palladium on charcoal (450 mg) and 9 mL of 2 *M* hydrochloric acid at 30–40°C until hydrogen uptake ceased. Filtration and evaporation of the reaction mixture afforded naphthol **11** (HCl) in quantitative yield (Table 4); ^{1}H nmr (DMSO-d_6): 1.3–3.6 (m, 7H, C(5–8)H), 6.3 (s, 1H, C(1)H), 6.4 (dd, 1H, C(3)H), 6.7 (d, 1H, C(4)H), 8.2 (br, 3H, NH_3^+), 9.0 (br, 1H, OH); ms, *m/e* (relative intensity): 164 (8), 163 (39), 146 (68), 120 (100).

Acknowledgements

We are grateful to the Comisión Asesora de Investigación Científica y Técnica for financial support. We thank Dr. Carlos Jaime for helpful discussions about MM2 calculations.

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