(*S*)-Spiro[(1,3-diazacyclopent-1-ene)-5,2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)]: Resolution, Stereospecific Synthesis, and Preliminary Pharmacological Characterization as a Partial α-Adrenergic Agonist

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Recently, we reported on the design, synthesis, and structure−activity relationships of a series of spiroimidazolines endowed with α-adrenergic agonist activities. Among the compounds described, (*R*,*S*)-spiro(1,3-diazacyclopent-1-ene)-[5,2′](7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene) fumarate (**5*RS***) was chosen for further development as a venotonic agent. The resolution of this compound, as well as the pharmacological characterization of the enantiomers, stereospecific synthesis of eutomer (**5*S***, S 18149), and determination of absolute configuration by single-crystal X-ray diffraction analysis, are described.

Introduction

Recently, we reported on the design, synthesis, and structure−activity relationships of a series of spiroimidazolines endowed with α adrenergic agonist activities.[1] Among the compounds described, (*R*,*S*)-spiro(1,3-diazacyclopent-1-ene)-5,2′]-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene) fumarate (**5*RS***) was chosen for further development as a venotonic agent. Indeed, this compound is the prototype of a venospecific constrictor as it is able to constrict the saphenous vein of the dog without noticeable effects on the mean arterial pressure.

As this compound contains an asymmetric center at carbon 5-2′, it was important to assess the influence of chirality on the pharmacological properties of compound **5*RS***. In fact, regulatory agencies are increasingly concerned[2] by the administration of racemic compounds as drugs if no benefit can be related to the presence of each of the enantiomers. In addition, it is preferential to investigate whether the observed pharmacological properties reside in one enantiomer, an eventuality which could accelerate development.[3]

We now report on the resolution of this racemic compound, describe the preliminary pharmacological characterization of the most active enantiomer, and document the determination of its absolute configuration as well as its stereospecific synthesis.

Chemistry

The resolution of the two enantiomers of **5*RS*** was initially achieved by recrystallization of the dibenzoyl-L-tartaric salt in ethanol. Resolution was monitored by chiral HPLC. After three crystallizations the enantiomeric purity exceeded the limit of detection of the analytical method (ee >96%), the salt was decomposed in strong basic media, and the free base was transformed into the fumarate in 2-propanol to afford **5*R***. The opposing enantiomer was obtained by evaporation of the initial filtrates, followed by decomposition of the salt by the addition of a strong base and dichloromethane extraction. The crude free base was combined with an equimolecular amount of the D enantiomer of dibenzoyltartaric acid and crystallized twice in ethanol to afford the opposite enantiomer **5*S*** in ee >96%.

Our approach toward the stereospecific synthesis of **5*S*** was inspired by the work of Weinges et al.[4] who synthesized (*R*)-α-methylphenylalanine by a stereospecific Strecker synthesis using (1*R*)-phenylethylamine as chiral inducer. Stereospecific Strecker synthesis[5] have been successfully exemplified in recent years starting mainly from aromatic aldehydes;[6−13] however comparatively little success has been achieved starting from ketone substrates.[14,15] In our case (Scheme 1) we used the 7-methyl-2-tetralone as template, a ketone with little difference between its two arms: a benzyl residue and a phenylethyl residue. The reaction proceeded cleanly and in high yield to give a diastereoisomerically pure solid endowed with the desired 2*S* configuration. As the Strecker reaction is a reversible process, the complete diastereoselectivity observed during this procedure is probably linked to the crystallization of one pure diastereoisomer exhibiting much lower solubility than the other and therefore displacing the whole equilibrium in favor of the production of this sole enantiomeric adduct. In this respect, it is worth mentioning that improvements of yield were obtained by increasing the water content of the solvent mixture, leading to better recovery of the poorly soluble product. Attempts to characterize the presence of the other diastereoisomer in the mother liquors failed. As expected, the mirror-image reaction starting from (1*S*)-phenylethylamine led, in the same conditions, to **5*R*** in comparable yields (data not shown).

Biology

The two enantiomers **5*S*** and **5*R*** as well as the racemic **5*RS*** described above were tested for their biological activity in the pithed rat (*in vivo*) and on contractibility of isolated canine saphenous veins and femoral arteries (*in vitro*). The pithed rat assay allows quantitative determination of the impact of the tested

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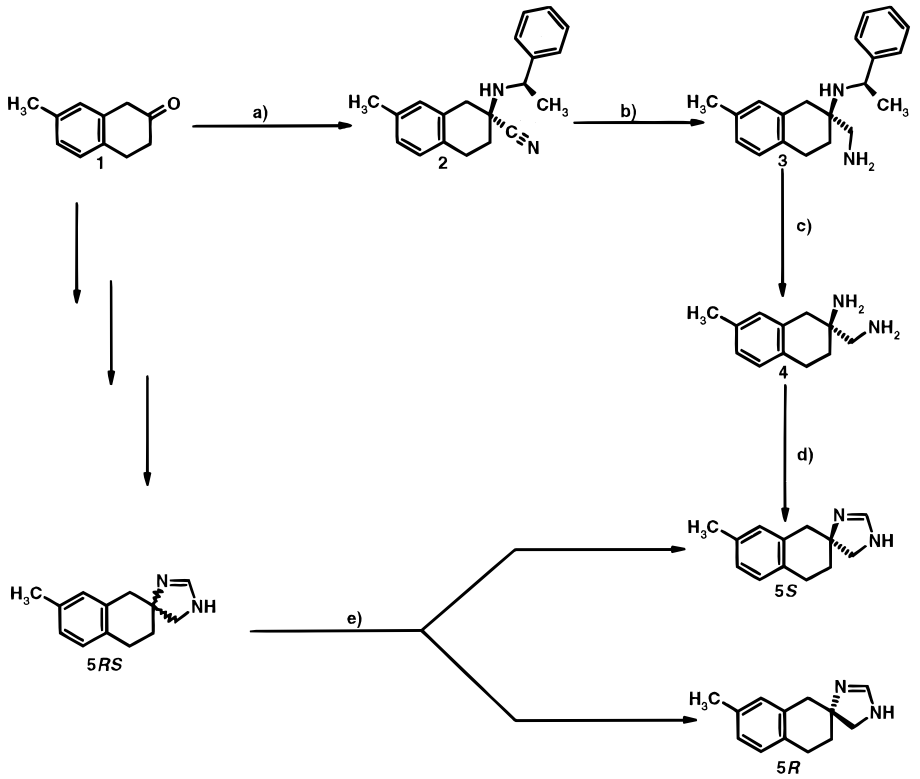
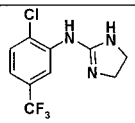
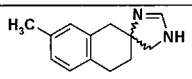
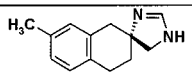
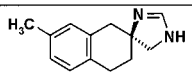
Scheme 1[a]



[a] Reagents and conditions: (a) (*R*)-α-methylbenzylamine, NaCN, AcOH, EtOH, MeOH, H_2O, 94% yield; (b) $LiAlH_4$, THF, 93% yield; (c) H_2, 5% Pd/C, MeOH, 78% yield; (d) HC(=NH)NH_2·AcOH, EtOH, 87% yield; (e) dibenzoyl-D-tartaric acid or dibenzoyl-L-tartaric acid, EtOH, 11 and 6% yield, respectively.

Table 1. *In Vitro* and *in Vivo* α-Adrenergic Activity of Compounds **5**

Cpd #	Structure	Pithed rat: Control C_{20}[a]	Pithed rat: Control Max[b]	Pithed rat: $C_{20antag}$/$C_{20control}$ Praz[c]	Pithed rat: $C_{20antag}$/$C_{20control}$ Yohim[c]	Isolated blood vessel: Femoral Artery EC_{50}[d] (μM)	Isolated blood vessel: Femoral Artery E_{max}[e]	Isolated blood vessel: Saphenous Vein EC_{50}[d] (μM)	Isolated blood vessel: Saphenous Vein E_{max}[e]
6	 **St 587**	8.6±1.6	129±4	16	1.8	10.9±7.9	19.7±2.1	2.02±0.77	54.4±10.2
5RS		6.7±0.6	112±2	6.1	7.9	>3	7.7±2.2	0.36±0.01	68.5±8.6
5R		44.8±4.6	109±5	20	12	>3	8.4±2.8	2.8±0.39	39.4±10.2
5S		5.8±1.5	106±4	6.5	4.2	>3	15.8±3	0.22±0.05	78.3±9.1

[a] Concentration which increases the arterial pressure by 20 mmHg in the pithed rat, expressed in μg/kg iv (mean ± SEM, $n = 5$). [b] Maximal pressure response (mean ± SEM) caused by the agonist, expressed in mmHg (the maximum obtained with phenylephrine is 150 mmHg). [c] Ratio of C_{20} obtained in the absence or presence of 0.1 mg of prazosin or 1 mg of yohimbine. [d] EC_{50} value for the agonist in the isolated blood vessel shown in μM (mean ± SEM, $n = 6-12$). [e] E_{max} = maximal contractile response obtained with the agonist expressed as percentage (mean ± SEM) of the maximal contraction to KCl (100 mM) in the blood vessel indicated.

compounds on the vascular tone defined by the dose (in μg/kg iv) which increases the arterial blood pressure by 20 mmHg (C_{20} in Table 1). Additionally, the maximal pressor response caused by the agonist (Max), expressed in mmHg, is an indication of the efficacy of the tested compounds. In the same assay, the use of selective α_1- and α_2-adrenoceptor antagonists (prazosin and yohimbine) in the presence of the tested compounds allows the definition of a C_{20} ratio (Praz and Yohim, respectively), which are indicative of the contribution of α_1- and α_2-adrenergic mechanisms to the pressor response. The *in vitro* evaluation allows the comparison in terms of affinity (EC_{50}) and efficacy (E_{max}) on two types of vascular beds which might be responsible for either the expected therapeutic efficacy (saphenous vein) or the potential side effect (femoral artery).

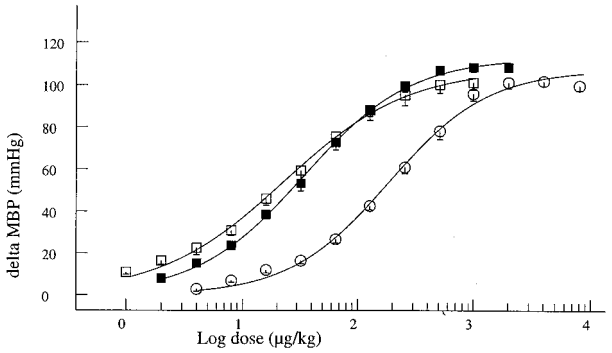


Figure 1. Effect of compounds **5** in the pithed rat. Dose−response effect of **5*RS*** ($n = 5$) (■), **5*R*** ($n = 5$) (○), and **5*S*** ($n = 8$) (□) on mean arterial blood pressure (MBP) in the pithed rat. Data are shown as means ± SEM.

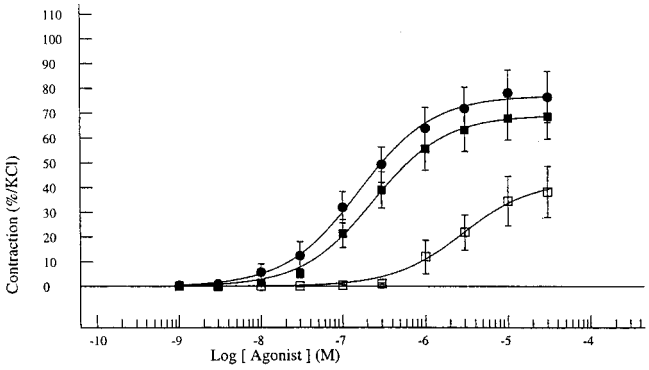


Figure 2. Effect of compounds **5** on the dog saphenous vein without Endothelium. Contractile activity of increasing concentrations of **5*RS*** (■), **5*R*** (□), and **5*S*** (●) on the dog saphenous vein without endothelium. Data are the means ± SEM of 6−12 experiments.

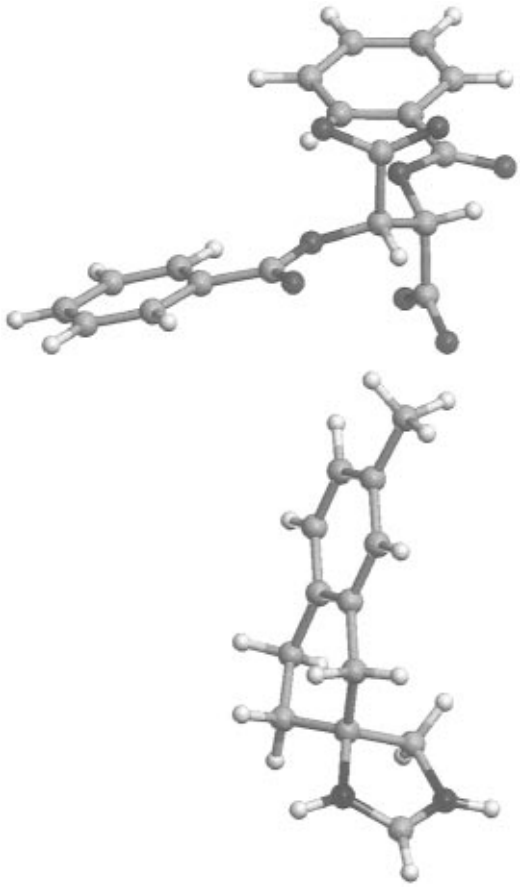


Figure 3. Single-crystal X-ray structure of **5*S*** as a dibenzoyl-D-tartaric acid salt.

Results and Discussion

The results of the biological evaluations of compounds **5** are presented in Figures 1 and 2, as well as in Table 1. In the pithed rat (Figure 1), the three compounds were administered in cumulative doses iv to three groups of rats. These doses caused dose-related pressor responses. The effect of **5*S*** was comparable to that of **5*RS***. **5*R*** was significantly less potent than **5*RS*** and **5*S*** but caused comparable increases in arterial blood pressure at the highest doses used. The maximal pressor response was reached with **5*R*** at 4 mg/kg but with **5*RS*** and **5*S*** at 1 mg/kg. The experiments were repeated using the same cumulative doses after blockade of α_1-adrenoceptors with prazosin (100 μg/kg iv 10 min before) and after blockade of α_2-adrenoceptors with yohimbine (1 mg/kg iv 10 min before). Both the α_1- and α_2-adrenoceptor antagonists led to significant and comparable displacement of the dose−response curve to the right (data not shown). Prasozin also decreased the maximal pressor response induced by compounds **5**. The maximal responses were reached with **5*RS*** and **5*S*** at 1 mg/kg in the control group and at 4 mg/kg in both prazosin- and yohimbine-treated animals. These experiments offer *in vivo* evidence that **5*S*** is the eutomer of the racemic mixture **5*RS*** and acts as a partial agonist at both α_1- and α_2-adrenoceptors.

In dog femoral arteries, compounds **5** evoked weak concentration-dependent contractions (data not shown); the maximal responses and the affinities of the three compounds were not significantly different and averaged less than 16% of the responses obtained with KCl (100 mM). In dog saphenous veins, compounds **5** evoked concentration-dependent contractions (Figure 2); the maximal response and the affinities of the three compounds were in the following order of potency: **5*S*** > **5*RS*** ≫ **5*R***, indicating that in this tissue also, **5*S*** is the active enantiomer of **5*RS***. A comparison of the maximal effects of **5*S*** in the dog saphenous vein (78.3 ± 9.1%) and femoral artery (15.8 ± 3%) shows that the response was significantly ($p \leq 0.001$) greater in the vein than in the artery.

In our previous report,[1] we discussed the use of an empirical ratio between the C_{20} value in the pithed rat and the EC_{50} value obtained in the vein as a discriminator in the search of venous specific compounds. When the same calculations were made from the number displayed in Table 1, the following order of venous specificity is obtained **5*S*** (26) > **5*RS*** (19) > **5*R*** (16), confirming that all the favorable properties of the racemic (potency and selectivity) are present in only one enantiomer: **5*S***. As all the curves were parallel, one can speculate that the residual activity of **5*R*** in these assays is linked to the likely presence of small amounts of **5*S*** (<2% according to the accuracy of the analytical method) in "pure" *R* enantiomer samples.

The absolute configuration of **5*S*** was obtained through single-crystal X-ray diffraction analysis performed on the dibenzoyl-D-tartaric acid salt, by Dr. C. Pascard at ICSN (Gif sur Yvette). The absolute configuration of the tartaric acid being known, the configuration of carbon 2 is *S* (Figure 3). One atom of hydrogen appeared on each nitrogen atom, the two C−N bonds

in the imidazoline are equal (1.29 Å), and the N1 nitrogen atom is in equatorial position as anticipated in the design process.[1] Additionally, two hydrogen bonds joined each of the nitrogens to two oxygen atoms belonging to different molecules N1−H−O (2.73 Å) and N3−H−O (2.76 Å). It is worth mentioning that the absolute configuration disclosed in the eutomer is the same as that seen for SDZ-NVI 085[16] and SK&F l-89748,[17] two other α-adrenoceptor agonists exhibiting a comparable chiral center which is in fact absent in the endogenous hormones adrenaline and noradrenaline.

In conclusion, our quest for a potent and selective α-adrenoceptor agonist endowed with a particular venous selectivity has terminated with the selection of **5*S*.** The compound is currently under development as S 18149 to test the initial hypothesis that such compounds might be useful in the treatment of venous disease and the prevention of ulcers. Further characterization of the pharmacological properties of **5*S*** has already appeared in abstract forms.[18,19]

Experimental Section

Biology. Methods (pithed rat and isolated blood vessels) described in ref 1 were used without changes.

Chemistry. Reagents were commercially available and of synthetic grade. ^{1}H NMR spectra relative to TMS were recorded on Bruker 200 or 400 MHz spectrometers. Infrared spectra were obtained as Nujol emulsion, on a Bruker Fourier transform spectrometer. All new substances were homogeneous in TLC and exhibited spectroscopic data consistent with the assigned structures. Elemental analyses (C, H, N) were performed on a Carlo Erba 1108 instrument and agree with the calculated values within the ±0.4% range. Melting points were obtained on a Reichert hot stage microscope and are uncorrected. Silica gel 60, Merck 230−400 mesh, was used for both flash and medium-pressure chromatography. TLC were performed on precoated 5 × 10 cm, Merck silica gel 60 F254 plates (layer thickness 0.25 mm). Gas chromatography was performed on a 5890 Hewlett-Packard instrument with a CP Sil 5 CB column (50 m × 0.32 mm), on column injection (150 °C), FID detection (280 °C), *t*° raising from 100 to 250 °C at the rate of 15 °C/min and then holding this *t*° for 20 mn. Chiral HPLC were performed on a Hewlett-Packard series 1050 instrument equipped with a UV variable detector set at 220 nm and a DAICEL Chiralpack AS column eluted with a mixture of *n*-heptane/2-propanol/diethylamine (920/80/0.5).

(*R*)-Spiro[(1,3-diazacyclopent-1-ene)-5,2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)], Fumarate (5*R*). Resolution by Formation of Diastereoisomeric Salts. A solution of dibenzoyl-L-tartaric acid (9.41 g, 25 mmol) in ethanol (200 mL) was added to a stirred solution of (*R*,*S*)-spiro-[(1,3-diazacyclopent-1-ene)-5,:2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)][1] (**5*RS***, 5 g, 25 mmol) in ethanol (170 mL). The solution was filtered and concentrated under reduced pressure to provide an amorphous residue which was dissolved in boiling ethanol (550 mL). After cooling at 20 °C for 2 h and then at 5 °C overnight, crystals formed which were filtered, washed with a small amount of cold ethanol, and dried under reduced pressure (4.7 g, ee: 76%). This crystallization procedure was repeated three times under the same conditions (minimum amount of ethanol to ensure the complete dissolution ≅ 100 mL/g) until enantiomeric purity was superior to 98%, as indicated by chiral HPLC. The pure diastereoisomeric salt (1.3 g, ee: ≫96%) was taken up in water (10 mL) and treated with concentrated aqueous NaOH (5 mL); the free base was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated to yield a white solid (0.44 g, 2.2 mmole). The solid was dissolved in boiling 2-propanol (20 mL) in the presence of fumaric acid (0.255 g, 2.2 mmol) and the resulting solution filtered hot. A minimum of diethyl ether was added until a haze appeared; the system was cooled to 5 °C and left overnight. The desired compound was obtained after filtration and drying, as colorless crystals (0.46 g, 6%): mp 163−164 °C; ^{1}H NMR (DMSO-d_6) δ 8.5−11.5 (m exchanged with D_2O), 8.25 (s, 1H), 7 (d, 1H), 6.95 (dd, 1H), 6.9 (d, 1H), 6.45 (s, 2H), 3.55 (AB system, 2H), 2.95 (AB system, 2H), 2.7−2.9 (m, 2H), 2.25 (s, 3H), 1.8−2.1 (m, 2H); $[\alpha]^{20}_D = +52°$ (*c* = 1, ethanol 95%). Anal. ($C_{13}H_{16}N_2 \cdot C_4H_4O_4$) C, H, N.

(*S*)-Spiro[(1,3-diazacyclopent-1-ene)-5,2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)], Fumarate (5*S*). The compound was prepared as described for the *R* enantiomer. (*R*,*S*)-Spiro[(1,3-diazacyclopent-1-ene)-5,2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)] (**5*RS***, 3 g, 15 mmol, ee: 50%) was employed as starting material, resulting from the neutralization with aqueous NaOH, of the mother liquors from the resolution of the *R* enantiomer and using dibenzoyl-D-tartaric acid (5.65 g, 15 mmol) as chiral agent. After three crystallizations in ethanol (100 mL/g), the pure diastereoisomeric salt was neutralized and the free base converted to the fumaric acid salt. The title compound was isolated as colorless crystals (0.51 g, 11%), mp 163−165 °C. Spectroscopic characteristics were identical to those of the *R* enantiomer: $[\alpha]^{20}_D$ −53° (*c* = 1, ethanol 95%). Anal. ($C_{13}H_{16}N_2 \cdot C_4H_4O_4$) C, H, N.

7-Methyl-3,4-dihydro-(1*H*)-naphthalen-2-one (1). Step a: *m*-Tolylacetyl Chloride. Thionyl chloride (984 g, 7.3 mol) was added to a solution of *m*-tolylacetic acid (**1**, 1,000 g, 6.66 mol) in toluene (3 L), while the temperature was maintained at 50 °C. At the end of the addition, the reaction mixture was heated at 80−85 °C until the gas evolution ceased. The solution was then cooled at 40 °C and the solvent carefully removed under reduced pressure. The acid chloride was used without further purification in the following step.

Step b: 7-Methyl-3,4-dihydro-(1*H*)-naphthalen-2-one (1). *m*-Tolylacetyl chloride (1.000 g, 5.9 mol) in CH_2Cl_2 (3.5 L) was added dropwise to a stirred solution of $AlCl_3$ (925 g, 6.95 mol) in CH_2Cl_2 (7.5 L) at 0 °C. At the end of the addition, the reaction mixture was maintained at 0 °C for 15 min and then lowered to −40 °C. Ethylene (468 g, 16.7 mol) was bubbled slowly (430 g/h) into the mixture while the temperature was kept below −30 °C. Reaction progress was followed by gas chromatography. When starting material concentration was below 5%, the reaction mixture was poured over a mixture of water and ice (50/50, 18 kg) while the temperature was kept in the 15−20 °C range. The mixture was diluted with CH_2Cl_2 (4.5 L). The phases were separated, the aqueous solution was extracted with more CH_2Cl_2, and the pooled organic phases were washed with aqueous $NaHCO_3$ until neutrality. The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure. The solid residue was washed with diisopropyl ether to remove the isomeric 1,2,3,4-tetrahydro-5-methyl-2(1*H*)-naphthalenone and dried under reduced pressure (445 g, 47%), mp 61 °C with decomposition.

7-Methyl-2(*S*)-[[1(*R*)-phenylethyl]amino]-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (2). 1(*R*)-Phenylethylamine (757 g, 6.24 mol) was added dropwise, followed by acetic acid (375 g, 6.24 mol) to a solution of 7-methyl-3,4-dihydro-(1*H*)-naphthalen-2-one (**1**) (1000 g, 6.24 mol) in a mixture of ethanol, methanol, and water (6 L, 4/1/1), at such a rate that the temperature did not exceed 35 °C. A solution of sodium cyanide (337 g, 6.86 mol) in water (1.5 L) was then added dropwise and the reaction mixture heated to 40 °C for 1 h during which the suspension became difficult to stirr. Water (4.5 L) was added, and the mixture was stirred for 2.5 h at 40 °C, followed by 24 h at room temperature. Water (3 L) was added again, and the suspension was cooled at −15 °C for 1 h, filtered, rinsed with ice cold ethanol, and dried under reduced pressure to afford a white solid (1700 g, 94.5%): mp 112 °C; ^{1}H NMR ($CDCl_3$) δ 7.1−7.4 (m, 5H), 7 (d, 1H), 6.9 (dd, 1H), 6.4 (d, 1H), 4.25 (q, 1H), 3 (m, 2H), 2.6 (AB system, 2H), 2.2 (s, 3H), 2−2.3 (m, 2H), 1.65 (m exchanged with D_2O), 1.45 (d, 3H).

[2(*S*)-(Aminomethyl)-7-methyl-1,2,3,4-tetrahydronaphthalen-2-yl][1(*R*)-phenylethyl]amine, Dihydrochloride (3). A solution of 7-methyl-2(*S*)-[1(*R*)-phenylethyl]amino]-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (**2**, 1000 g, 3.44

mol) in THF (7 L) was added dropwise to a suspension of $LiAlH_4$ (304 g, 8 mol) in THF (13 L) at such a rate that gas evolution remained controlable and the temperature did not exceed 20 °C. The suspension was stirred at 20 °C for 3 h until the starting material had disappeared on TLC (methanol/acetone, 80/20). The reaction mixture was hydrolyzed by careful and succesive additions of water (0.3 L), 2 N NaOH (0.35 L), and water (0.575 L) while the temperature was maintained below 20 °C. The solid was filtered and washed with THF (2 × 1 L), and the pooled organic solutions were evaporated under reduced pressure. The residue was taken up in ethyl acetate (6.5 L), and the hydrochloride salt was formed by addition of 3.5 N HCl in ethyl acetate (2 L) at 0 °C. The solid was filtered, washed with ethyl acetate, and dried under reduced pressure to afford a white solid (1180 g, 93%): mp 190 °C; ^{1}H NMR (DMSO-d_6) δ 10.15 (br s exchanged with D_2O, 2H), 8.74 (br s exchanged with D_2O, 3H), 7.80 (br s, 2H), 7.46 (br s, 3H), 6.96 (AB system, 2H), 6.50 (s, 1H), 3.61−3.32 (m, 2H), 3.13−2.61 (m, 4H), 2.39−1.92 (m, 3H), 2.17 (s, 3H), 1.77 (d, 3H).

2(*S*)-(Aminomethyl)-7-methyl-1,2,3,4-tetrahydronaphthalen-2-ylamine, Dihydrochloride (4). A solution of [2(*S*)-aminomethyl-7-methyl-1,2,3,4-tetrahydronaphthalen-2-yl][1(*R*)-phenylethyl]amine, dihydrochloride (**3**) (1000 g, 2.74 mol) in methanol (12 L) was hydrogenated at 20 °C under 1 bar of hydrogen and in the presence of Pd (5% Pd/C, 50% humidity, 100 g). Each time the flow of hydrogen decreased (twice), the suspension was filtered and a new batch of catalyst (5% Pd/C, 50% humidity, 100 g) was added to the reactor. At the end of the theoretical absorption (68 L), the catalyst was filtered off and the solution was concentrated under reduced pressure. The residue was stirred with hot acetone (5 L), cooled at 0 °C, and filtered to afford, after drying under reduced pressure, a white solid (559 g, 78%): mp 250 °C; ^{1}H NMR (DMSO-d_6) δ 8.87 (br s exchanged with D_2O, 6H), 6.97 (dd, 2H), 6.9 (s, 1H), 3.21 (AB system, 2H), 3.03 (br s, 2H), 2.66 (AB system, 2H), 2.21 (s, 3H), 2.06 (t, 2H).

(*S*)-Spiro[(1,3-diazacyclopent-1-ene)-5,2′-(7′-methyl-1′,2′,3′,4′-tetrahydronaphthalene)], Fumarate (5S). NaOH pellets (353 g, 8.83 mol) were added to a suspension of 2(*S*)-(aminomethyl)-7-methyl-1,2,3,4-tetrahydronaphthalen-2-ylamine, dihydrochloride (**4**, 1000 g, 3.8 mol), and formamidine acetate (491 g, 4.75 mol) in ethanol (15.7 L). The reaction mixture was stirred for 1 h at 20 °C, concentrated under reduced pressure, and then taken up in 1.5 N HCl (14 L) and extracted with ethyl acetate (2 × 2 L). The aqueous phase was brought to pH 12.5 by the slow addition of 10 N NaOH while the temperature was kept at 20 °C. The solid was filtered, washed with water, and dried under reduced pressure to afford a white powder (661 g, 87%), mp 182−183 °C. The fumarate salt was prepared quantitatively in ethanol or 2-propanol at the concentration of 1/15: mp 162−165 °C. Spectroscopic characteristics were identical to those of the compound obtained by the other route.

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Supporting Information Available: X-ray analysis data (5 pages). Ordering information is given on any current masthead page.

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