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Conformational Studies by Dynamic NMR. 93.[1] Stereomutation, Enantioseparation, and Absolute Configuration of the Atropisomers of Diarylbicyclononanes

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Received October 8, 2002

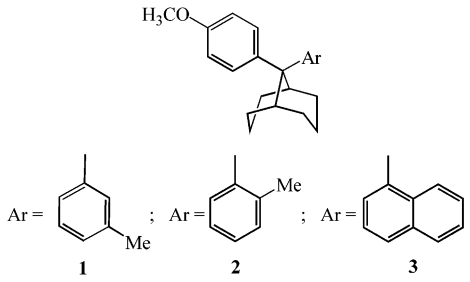
The structure of 9-(4-methoxyphenyl)-9-(3-methylphenyl) bicyclo[3.3.1]nonane (**1**) has been determined by single-crystal X-ray diffraction, and the rotation barriers about the two aryl−C9 bonds have been measured by variable temperature NMR spectroscopy in solution. In the case of 9-(4-methoxyphenyl)-9-(1-naphthyl)bicyclo[3.3.1]nonane (**3**), the barrier involving the naphthyl−C9 rotation was found to be so high as to allow the physical separation of the two atropisomers by enantioselective HPLC at ambient temperature: the absolute configuration could be established on the basis of the corresponding CD spectra. It was also observed that the Ar−C9 rotation barriers of monoaryl-substituted nonanes are much lower than those of the corresponding diaryl-substituted nonanes.

Introduction

Derivatives of 7,7-diaryl norbornanes have been shown[2] to adopt a face-to-face conformation (apical cofacial) of the two aromatic substituents, the opposite conformation of the diarylmethane derivatives where the aromatic rings are nearly orthogonal and display a propeller-like disposition.[3] In a number of such diaryl norbornanes, bearing a fluorine atom in the ortho position of the phenyl group, the rotational barriers about the 2-fluorophenyl to norbornane bond were determined by dynamic NMR spectroscopy.[4] The corresponding free energies of activation were found to lie in the range 16.2−17.2 kcal/mol, which implies that the two enantiomeric forms are stereolabile and cannot be separated at ambient temperature. In principle, restricted rotation should have been also observed for the second of the two aryl substituents, but this additional feature was not reported.[4]

We have been able to detect the rotation process of both aryl substituents in a quite similar type of compound, i.e., 9,9-diarylbicyclo[3.3.1]nonanes **1**−**3** (Chart 1). The striking observation is that the two rotation barriers are very similar, and quite small, in the case of **1** but extremely different in **2** and **3**. As a consequence, the latter compounds give origin to a pair of stable enantiomers (atropisomers) that, in principle, might undergo physical separation.

CHART 1



1 **2** **3**

It is interesting to outline that this represents a new case of nonbiaryl atropisomerism, which, up to now, has been reported for imides, oximes, tertiary aromatic amines, and *N*-aryl amides.[5]

Results and Discussion

X-ray diffraction (Experimental Section) as well as ab initio[6] and MM calculations[7] of **1** indicate that the two

(1) Part 92. Garcia, M. B.; Grilli, S.; Lunazzi, L.; Mazzanti, A.; Orelli, L. R. *Eur. J. Org. Chem*. **2002**, 4018. For Part 91, see: Grilli, S.; Lunazzi, L.; Mazzanti, A.; Pinamonti, M.; Anderson, J. E.; Ramana, C.V.; Koranne, P. S.; Gurjar, M. K. *J. Org. Chem*. **2002**, *67*, 6387.

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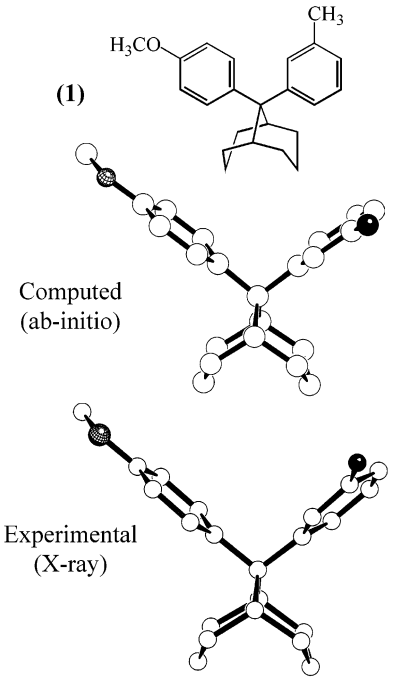
10.1021/jo0265378 CCC: $25.00
Published on Web 01/31/2003

SCHEME 1



aryl groups are cofacial (Scheme 1) and that there is not warping of the aromatic rings. Since the adopted structure has no element of symmetry (C_1 point group), derivative **1** appears as a chiral object in the crystalline state. Accordingly, the two molecules contained in the unit cell are in an enantiomeric relationship (atropisomers): one such atropisomer is shown in Scheme 1.

In solution, on the other hand, the rotation of the 3-methylphenyl group is sufficiently fast to make the two atropisomers interconvert rapidly at ambient temperature. The barrier involved in such an enantiomerization process was determined by monitoring the ^{13}C lines of 1,5-positions of the bicyclononane as a function of temperature (Figure 1). The corresponding single line broadens upon cooling and splits into a pair of signals at −96 °C since the corresponding carbons become diastereotopic when the rotation rate of the 3-methylphenyl ring is sufficiently slow. From a number of rate constants, determined at various temperatures by line shape simulation, a $\Delta G^{\ddagger}$ value of 10.8 kcal/mol was obtained (Table 1): as often observed in conformational processes, the $\Delta S^{\ddagger}$ value was found to be negligible,[8] thus making $\Delta H^{\ddagger} \approx \Delta G^{\ddagger}$ within the experimental uncertainty.

At −96 °C, also the rotation rate of the 4-methoxyphenyl becomes slow, making the corresponding pairs of ortho and meta carbons diastereotopic; this is a consequence of the asymmetry brought about by the simultaneous slow rotation of the 3-methylphenyl group mentioned above.

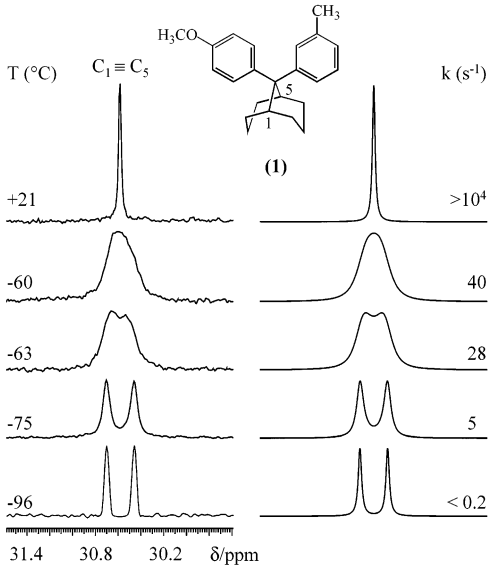


FIGURE 1. Experimental (left) and computed (right) variable temperature NMR spectra (75.45 MHz in CD_2Cl_2) of the carbons in 1,5-positions of the nonane moiety in derivative **1**.

TABLE 1. Barriers (in kcal/mol) for the Rotation of the 4-Methoxyphenyl Group in 1−3 and for the Enantiomerization Process (i.e., Rotation of the other Ar Groups) in 1−6[a]

compd	1	2	3	4	5	6
rotation	10.2	5.4	5.15			
enantiomerization	10.8	>25	>25	6.5	9.45	11.95

[a] Absolute experimental error = ±0.15 kcal/mol.

In Figure 2, the ^{13}C signal of the carbons in the position ortho[9] to the methoxy group is reported as a function of temperature. A line shape simulation provides the rate constants and, hence, the barrier for the rotation process of the 4-methoxyphenyl group. The corresponding value ($\Delta G^{\ddagger}$ = 10.2 kcal/mol) was found to be lower than the previous one: although the difference between the two barriers is not very large ($\Delta\Delta G^{\ddagger} = 0.6 \pm 0.1$ kcal/mol), it exceeds by far the experimental uncertainty. This is because the traces of Figures 1 and 2 were obtained from a unique sample at the very same temperature so that the experimental errors on the absolute temperatures do not affect the differences of the rate constants and, hence, the difference of the barriers. In these conditions, the only source of error is due to the small deviation from a perfect superimposition of the computed and experimental traces, which affected each $\Delta G^{\ddagger}$ by an amount not exceeding, in the present case, ±0.05 kcal/mol, in agreement with previous reports.[10]

(6) Calculations carried out at the RHF 6-31G* level as in the computer package Titan 1.0.5 (Wavefunction, Inc.; Irvine, CA).

(7) MMX force field, as implemented in the program PC Model V 7.5 (Serena Software, Bloomingtom, IN).

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(9) Assignment was performed by irradiating the ^1H methoxy signal (DPFGSE-NOE sequence) and observing the positive NOE experienced by the hydrogens in the ortho position. The line of the corresponding carbons was then identified by means of a heteronuclear two-dimensional correlation (gHSQC sequence).

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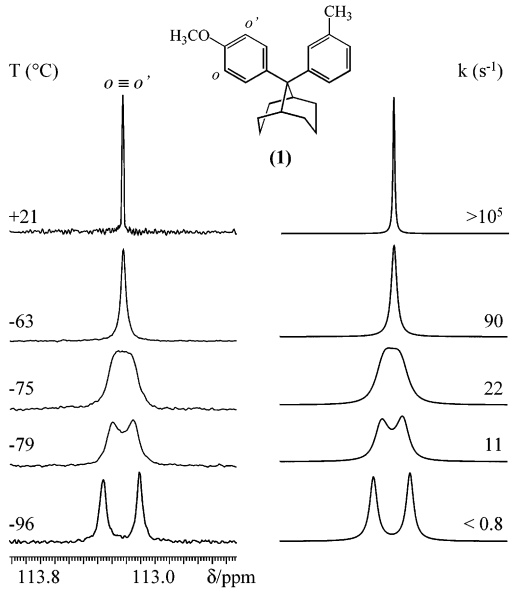
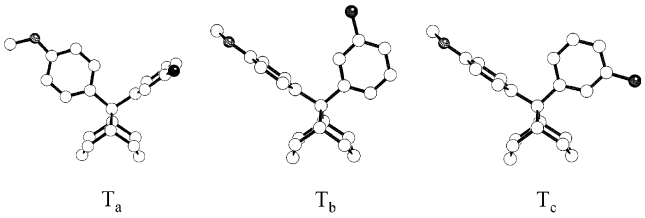


FIGURE 2. Experimental (left) and computed (right) variable temperature NMR spectra (75.45 MHz in CD_2Cl_2) of the carbons in the positions ortho to the MeO group in derivative **1**.

SCHEME 2



Both ab initio[6] and MM[7] calculations indicate that in derivative **1**, the transition state for the rotation process of the 4-methoxyphenyl group corresponds to the situation where this ring is essentially orthogonal to the plane of the other aryl substituent (i.e., 3-methylphenyl). The energy of this transition state is 9.9 or 9.6 kcal/mol (according to ab initio or MM computations, respectively) higher than that computed for the corresponding cofacial ground state (see Scheme 1). Both these computed values (the ab initio in particular) agree satisfactorily with the experimental barrier ($\Delta G^{\ddagger}$ = 10.2 kcal/mol as in Table 1). The ab initio-computed transition state of **1** is displayed as T_a in Scheme 2.

The rotation of the 3-methylphenyl ring, which corresponds to an enantiomerization process, can take place, in principle, according to two alternative pathways. For, the transition state (where the ring is rotated by 90° with respect to the situation of the cofacial ground state shown in Scheme 1) can have the 3-methyl group either oriented toward the 4-methoxy phenyl ring (as shown in Scheme 2, T_b) or oriented in the opposite direction (Scheme 2, T_c). The relative energy of the transition state T_c (10.4 kcal/mol in both the ab initio and MM computations) is slightly higher than that of the alternative transition state T_b (10.2 or 9.8 kcal/mol, respectively, in the ab initio or MM computations). This suggests that the enantiomerization process occurs, probably, according to the latter pathway, because of its lower energy (in any case, all the computed values match satisfactorily the experimental barrier of 10.8 kcal/mol, as in Table 1). Also, the computation of the barrier for the enantiomerization pathway involving the transition state T_b predicts a value slightly higher than that computed for the rotation of the 4-methoxyphenyl ring involving the transitions state T_a. The related energy differences are 0.3 kcal/mol in the case of ab initio calculations and 0.2 kcal/mol in the case of MM calculations, a result in agreement with the trend observed experimentally ($\Delta\Delta G^{\ddagger}$ = 0.6 kcal/mol).

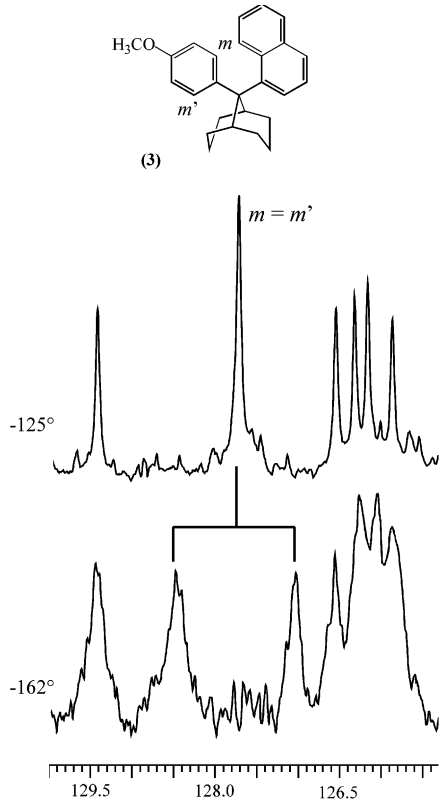


FIGURE 3. Temperature dependence of the NMR spectrum (100.6 MHz in $CHF_2Cl/CHFCl_2$) of the carbons in the positions meta to the MeO group in derivative **3**.

When the 3-methylphenyl substituent of **1** is replaced by the bulkier 2-methylphenyl group (compound **2**) or by the analogous 1-naphthyl moiety (compound **3**), a dramatic change occurs in the values of the rotation barriers. The barrier for the rotation of the 4-methoxyphenyl group is lowered so much (5.4 and 5.15 ± 0.15 kcal/mol in **2** and **3**, respectively, as in Table 1) that the spectra had to be recorded below −160 °C in order to detect anisochronous ^{13}C lines for the ring carbons: an example is reported in Figure 3 for the carbon lines in the meta position to the MeO group[11] in derivative **3**. On the contrary, the rotation barriers of the 2-methylphenyl in **2** and 1-naphthyl in **3** (corresponding to an enantiomerization process) become so high that not even at +180 °C an appreciable exchange broadening effect could be observed for the two lines of the carbons in positions 1 and 5 of the bicyclononane ring. This means that the

(11) Assignment of ref 9 indicates that the shift of the two carbons in position ortho to the methoxy group is about 113 ppm: as a consequence, the other aryl CH line, corresponding to a pair of equivalent carbons, had to be assigned to the meta carbons (shift at about 128 ppm).

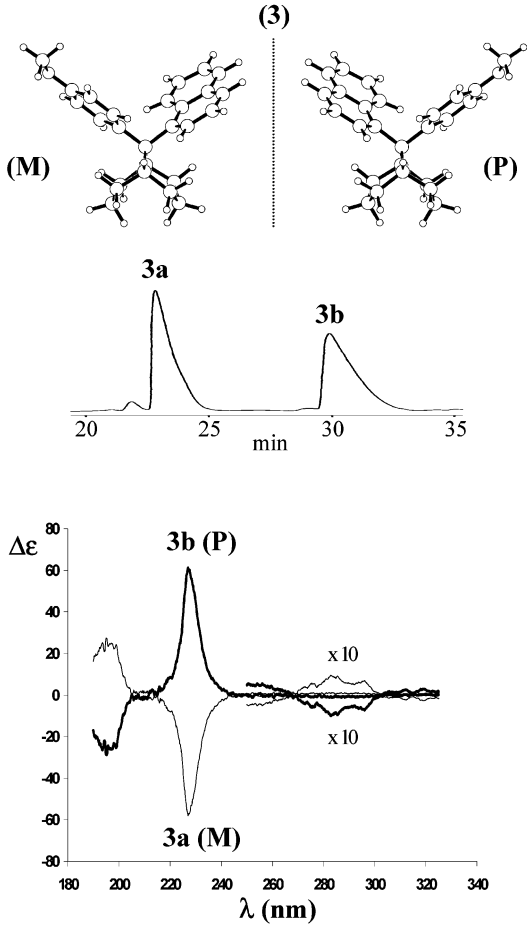


FIGURE 4. HPLC trace (top) and CD spectra (bottom) of the atropisomers of **3**. The absolute configuration **M** has been assigned to the first eluted atropisomer (**3a**) (see text).

corresponding enantiomerization barrier must be larger than 25 kcal/mol (Table 1) and, consequently, the atropisomers of **2** and **3** can be considered to be configurationally stable, having a half-life expected to be longer than a week at ambient temperature. This is because the steric requirements of 2-methylphenyl and of 1-naphthyl substituents in **2** and **3** are significantly larger than that of 3-methylphenyl in **1**, so the hindrance to the related rotation process (enantiomerization) becomes much higher in **2** and **3** with respect to **1**.[12]

This circumstance allowed us to perform a physical separation of the enantiomers of both **2** and **3** by means of an enantioselective column (see Experimental Section): in Figure 4 the HPLC trace showing evidence of such a separation is reported for the case of **3**. In the same picture are also reported the CD spectra displaying the oppositely phased trends for the two atropisomers.

The assignment of the absolute configuration could be best achieved by the X-ray Bijovet method, provided that a heavy atom is present in the molecule. Since no such an atom is available in compound **3**,[13] we used the alternative approach, based upon the interpretation of the corresponding CD spectra. It is well-known that CD spectroscopy has become a very effective tool, as reliable as the X-ray Bijovet method, for obtaining stereochemical assignments.[14] In particular, the coupled oscillator approach has been developed in the simple qualitative exciton chirality rules by Nakanishi et al.[15] and has been extensively applied to various organic molecules[16] as a microscale method to determine the absolute configuration in a nonempirical manner. We shall show that the CD spectrum of the first eluted enantiomer **3a** (full trace of Figure 4) can be analyzed by means of the above rules, thus leading to a reliable assessment of the absolute configuration. In this spectrum, the characteristic features of the 1-naphthyl chromophore[17] are clearly evident in that a weak, positive ($\Delta\epsilon$ +0.9) structured band at 285 nm and a very intense, negative ($\Delta\epsilon$ −56) band at 225 nm are observed.

These Cotton effects are certainly due to the ^1L_a and ^1B transitions,[17] polarized along the short and long axes of the naphthalene chromophore, respectively. Below 220 nm the absorption due to the *p*-methoxyphenyl chromophore,[18] in particular the ^1B transition of this moiety (λ 195 nm, $\Delta\epsilon$ +27), is also observed. There are therefore two chromophores (1-naphthyl and *p*-methoxyphenyl) that possess strongly allowed transitions with a known polarization. In addition, these chromophores are in a definite disposition with respect to each other, thus representing a typical case of exciton optical activity,[15] so that the CD data can be analyzed using this model. In particular we can limit our analysis to the 260−210 nm spectral region, i.e., the range where the ^1B transition of the naphthalene chromophore occurs. In this way we can relate the sign of this Cotton effect to the absolute configuration by making use of the exciton model. The naphthalene transition couples with the allowed transitions of the *p*-methoxyphenyl chromophore, in particular the very intense ^1B transition, around 195 nm, leading to the strong Cotton effects are observed at 225

(12) The lower barrier observed for the rotation of the 4-methoxyphenyl group in **2** and **3** with respect to **1** (see Table 1) may be a consequence of an increase in the energy of the ground state because of the molecular crowding.

(13) Contrary to the case of the unhindered compound **1**, we were unable to grow single crystals appropriate for X-ray diffraction in the case of the hindered derivatives **2** and **3** (i.e., the compounds displaying atropisomerism at ambient temperature). Thus, even if we had had introduced a heavy atom into compound **3**, we would have been quite unlikely to obtain crystals suitable for X-ray diffraction.

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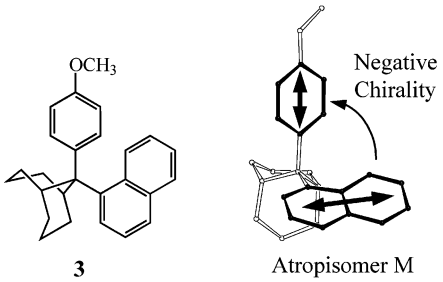
(17) Michl, J.; Thulsturp, E. W. *Spectroscopy with Polarized Light*; VCH: New York, 1986.

(18) Absorption and CD data for such chromophore can be found in: Rosini, C.; Spada, G. P.; Proni, G.; Masiero, S.; Scamuzzi, S. *J. Am. Chem. Soc.* **1997**, *109*, 5506.

SCHEME 3

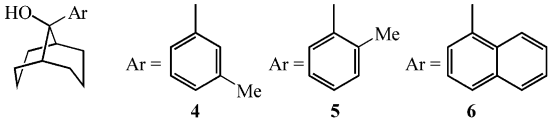


and 195 nm. The high intensity of the CD spectrum is in agreement with its exciton coupling origin, taking into account the well-known[17] high values of the extinction coefficients of the two absorption bands involved. This transition can be described[19] by two orthogonal dipoles (located in the plane of the benzene ring and at the center of it), one being directed along the O−C9 axis and the other perpendicular to it: the former is labeled longitudinal dipole and the latter transverse dipole. It is very important to observe that the *p*-substituted benzene group rotates very rapidly at ambient temperature (as deduced by the barrier measured by NMR), so the transverse dipole of the benzene chromophore assumes all the possible dispositions with respect to the long axis of the naphthalene chromophore. As a consequence, these two dipoles do not give rise to exciton coupling, whereas the longitudinal chromophore remains always in the same relative disposition with respect to the long axis of the naphthalene. To interpret the CD allied to this naphthalene transition, it is therefore sufficient to study the coupling of these two latter transitions.

The negative sign of the 230 nm Cotton effect, together with the positive CD band at 195 nm (full spectral trace), shows that in the structure corresponding to the first eluted enantiomer, the two dipoles mentioned above define a negative chirality[16] (Scheme 3). This means that this antipode (**3a**) has the absolute configuration **M**, i.e., the structure reported on the left-hand side of Figure 4. Consequently, the **P** configuration[20] (indicated on the right-hand side of Figure 4) corresponds to the second eluted atropisomer (**3b**) exhibiting the bold CD spectral trace.

As previously mentioned, the enantiomerization barrier in **2** and **3** is so much higher than that in **1** due to the steric effect of the second rotating ring, which greatly enhances the energy of the rotational transition state. Support for this hypothesis is offered by the observation that replacement of the 4-methoxyphenyl by the OH group as in **4**−**6** (Chart 2) significantly reduces all the enantiomerization barriers, yielding $\Delta G^{\ddagger}$ values equal to 6.5, 9.45, and 11.95 kcal/mol, respectively (see Table 1). However, the barriers of compounds **5** and **6**, which have bulkier Ar substituents, are still higher than that of **4**; furthermore, it should be also noticed that the barrier measured for **6** is higher than that of **5**, indicating that the steric effect of the 1-naphthyl is larger than that of the 2-methylphenyl substituent, a difference that could not be appreciated in **2** and **3** since the corresponding barriers were too high to be measured.

CHART 2



Experimental Section

Materials. The reagents commercially available were distilled before the use except the solid 9-nonanone, which was used without further purification. Diethyl ether was dried over Na and benzophenone.

The synthesis of the bicyclo[3.3.1]nonane-9,9-diaryls followed a general procedure where the 9-nonanone was first reacted with the appropriate Grignard reagent to give the bicyclo[3.3.1]nonane-9,9-aryl alcohols **4**−**6**. The final products **1**−**3** were obtained directly from the corresponding alcohols by modifying a general procedure described in the literature.[4,21] In a 50 mL flask, a solution of halide (4.5 mmol in 10 mL of dry ether) kept in a nitrogen stream was added dropwise to a suspension of Mg turnings (4.5 mmol in 20 mL of dry ether). The mixture was gently refluxed for 1−2 h, and a solution of 9-nonanone (3 mmol in dry ether 10 mL) was slowly added to the resulting light yellow mixture. The reaction was kept refluxing for additional 2−4 h, cooled to room temperature, and finally stopped with a saturated solution of NH_4Cl. The mixture was extracted with ether (3 × 15 mL), and the collected organic layers were dried and concentrated at reduced pressure. The crude product was purified by a silica gel chromatography column (5:1 v/v petroleum ether/Et_2O) to give a white solid. The final yields of the intermediate alcohols ranged between 65 and 85% on the purified products. In the second step of the synthesis, a solution of pure alcohol (0.74 mmol) in 2 mL of anisole was added dropwise in a nitrogen stream to a solution of CF_3SO_3H (1 mmol) in 5 mL of anisole. The reaction was stirred at room temperature, and the solution turned slowly from light yellow to deep red. After overnight reaction, CH_2Cl_2 (50 mL) was added and the reaction stopped with water. The decolored mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the collected organic layers were washed with water, dried, and concentrated to reduced pressure for several hours in order to eliminate the anisole. Crystallization from 9:1 v/v petroleum ether/Et_2O yielded **1** (55%) as a white solid (single crystals, suitable for X-ray diffraction, were obtained from ethanol). Crude **2** and **3** were purified by a silica gel chromatography column (20:1 v/v petroleum ether/Et_2O) and eventually by a preparative TLC (5/1 petroleum ether/toluene) to yield 15−20% pure sticky solids.

9-(3-Methylphenyl)bicyclo[3.3.1]nonan-9-ol (4): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.00−2.17 (9H, bm), 2.31−2.68 (2H, m), 3.35−3.50 (1H, m), 3.79 (3H, s), 6.88 (2H, d, J = 9.1 Hz), 7.11−7.25 (2H, m), 7.43 (2H, d, J = 9.1 Hz), 7.45−7.56 (2H, m), 7.67−7.73 (1H, m), 7.82−7.88 (1H, m), 8.18 (1H, bd, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 50.29 MHz) δ 20.5 (CH_2), 23.3 (CH_2), 27.6 (CH_2), 30.7 (CH_2), 34.9 (CH_2), 37.1 (CH_2), 38.5 (CH), 50.5 (CH), 50.8 (C_q), 55.2 (CH_3), 113.5 (2CH), 122.8 (CH), 123.6 (CH), 125.2 (CH), 125.7 (2CH), 126.2 (CH), 126.9 (2CH), 129.0 (CH), 132.7 (C_q), 134.0 (C_q), 142.1 (C_q), 143.1 (C_q), 157.3 (C_q). Anal. Calcd for $C_{16}H_{22}O$: C, 87.60; H, 7.92. Found: C, 86.62; H, 7.95.

9-(2-Methylphenyl)bicyclo[3.3.1]nonan-9-ol (5): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.10−2.46 (14H, m), 2.37 (3H, s), 2.71−

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(20) Actually, the P and M descriptors define the chirality sense of the helix, i.e., a set of nonplanar four atoms. These descriptors are used in the nomenclature of biaryl compounds (see for instance: Gawley, R. E.; Aubè, J. *Principle of Asymmetric Synthesis*; Pergamon Elsevier Science: Oxford, UK, 1996; p 30) where the C_{Ar}−C_{Ar} bond defines the helix axis. In **3a** and **3b**, the helix axis refers to the torsion angle between C9 and the α-carbon of the naphthyl substituent.

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2.85 (1H, m), 3.78 (3H, s), 6.85 (2H, d, J = 9.1 Hz), 7.02−7.42 (6H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 20.1 (CH_3), 20.8 (CH_2), 23.1 (CH_2), 27.3 (CH_2), 30.5 (CH_2), 34.0 (CH_2), 37.1 (CH_2), 40.0 (CH), 50.4 (CH), 50.5 (C_q), 55.1 (CH_3), 113.3 (CH), 125.7 (CH), 126.2 (CH), 126.4 (CH), 126.8 (CH), 130.1 (CH), 136.0 (C_q), 142.1 (C_q), 144.9 (C_q), 158.3 (C_q). Anal. Calcd for $C_{16}H_{22}O$: C, 86.20; H, 8.81. Found: C, 86.19; H, 8.85. Mp = 68−69 °C.

9-(1-Naphthyl)bicyclo[3.3.1]nonan-9-ol (6): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.35−1.45 (1H, m), 1.62−1.75 (6H, m), 1.82−2.10 (4H, m), 2.54−2.68 (2H, m), 2.85 (2H, bs), 7.36−7.47 (3H, m), 7.68−7.76 (2H, m), 7.81−7.86 (1H, m), 8.84−8.90 (1H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz) δ 20.5 (CH_2), 21.1 (CH_2), 27.9 (CH_2), 30.2 (CH_2), 37.5 (CH), 77.0 (Cq), 124.2 (CH), 124.7 (CH), 125.0 (CH), 125.2 (CH), 127.8 (CH), 128.6 (CH), 129.1 (CH), 131.7 (Cq), 135.3 (Cq), 140.9 (Cq). Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.65; H, 8.29. Mp = 101−102 °C.

9-(4-Methoxyphenyl)-9-(3-methylphenyl)bicyclo[3.3.1]-nonane (1): ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 1.33−1.41 (2H, m), 1.64−1.71 (4H, m), 1.88−2.16 (6 H, m), 2.27 (3H, s), 3.19 (2H, bs), 3.71 (3H, s), 6.76 (2H, d, J = 8.8 Hz), 6.83 (1H, bd, J = 7.4), 7.07−7.13 (1H, m), 7.20−7.22 (2H, bm), 7.32 (2H, d, J = 8.8 Hz); ^{13}C NMR (CD_2Cl_2, 75.45 MHz) δ 21.9 (CH_2), 22.0 (CH_2), 22.3 (CH_3), 28.4 ($2CH_2$), 28.5 ($2CH_2$), 32.5 (2CH), 48.2 (C_q), 55.8 (CH_3), 114.4 (2CH), 123.8 (CH), 126.1 (CH), 127.5 (CH), 128.0 (2CH), 129.0 (CH), 138.7 (C_q), 141.1 (C_q), 149.3 (C_q), 157.5 (C_q). Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 86.22; H, 8.83. Mp = 121.5−121.8 °C.

9-(4-Methoxyphenyl)-9-(2-methylphenyl)bicyclo[3.3.1]-nonane (2): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.10−2.46 (14H, m), 2.37 (3H, s), 2.71−2.85 (1H, m), 3.78 (3H, s), 6.85 (2H, d, J = 9.1 Hz), 7.02−7.42 (6H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 20.1 (CH_3), 20.8 (CH_2), 23.1 (CH_2), 27.3 (CH_2), 30.5 (CH_2), 34.0 (CH_2), 37.1 (CH_2), 40.0 (CH), 50.4 (CH), 50.5 (C_q), 55.1 (CH_3), 113.3 (CH), 125.7 (CH), 126.2 (CH), 126.4 (CH), 126.8 (CH), 130.1 (CH), 136.0 (C_q), 142.1 (C_q), 144.9 (C_q), 158.3 (C_q). Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 86.19; H, 8.79.

9-(4-Methoxyphenyl)-9-(1-naphthyl)bicyclo[3.3.1]-nonane (3): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.00−217 (9H, bm), 2.31−2.68 (2H, m), 3.35−3.50 (1H, m), 3.79 (3H, s), 6.88 (2H, d, J = 9.1 Hz), 7.11−7.25 (2H, m), 7.43 (2H, d, J = 9.1 Hz), 7.45−7.56 (2H, m), 7.67−7.73 (1H, m), 7.82−7.88 (1H, m), 8.18 (1H, bd, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 50.29 MHz) δ 20.5 (CH_2), 23.3 (CH_2), 27.6 (CH_2), 30.7 (CH_2), 34.9 (CH_2), 37.1 (CH_2), 38.5 (CH), 50.5 (CH), 50.8 (C_q), 55.2 (CH_3), 113.5 (2 CH), 122.8 (CH), 123.6 (CH), 125.2 (CH), 125.7 (2CH), 126.2 (CH), 126.9 (2CH), 129.0 (CH), 132.7 (C_q), 134.0 (C_q), 142.1 (C_q), 143.1 (C_q), 157.3 (C_q). Anal. Calcd for $C_{26}H_{28}O$: C, 87.60; H, 7.92. Found C, 87.59; H, 7.89.

X-ray Diffraction: Crystal Data of 9-(4-Methoxyphenyl)-9-(3-methylphenyl)-bicyclo[3.3.1]nonane (1). $C_{23}H_{28}O$ (320.45), triclinic, space group P-1, Z = 2, Z primary = 1, a = 6.4293(12), b = 8.9518(17), c = 16.017(3) Å, α = 76.260(4), β = 83.808(4), γ = 88.737(4), V = 890.2(3) Å ^{3}, D_c = 1.195 g/cm^3, $F(000)$ = 348, μ_{Mo}= 0.071 mm^{-1}, T = 293 K, crystal size 0.4 × 0.2 × 0.05 mm. Data were collected using a graphite monochromated Mo Kα X-radiation (λ = 0.71073 Å); range 1.32° < θ < 30.06°. Of 10 997 reflections collected, 5167 were found to be independent (R_{int} = 0.0399), 2412 of which were considered as observed [$I > 2\sigma(I)$], and were used in the refinement of 218 parameters leading to a final R_1 of 0.0618 and a R_{all} of 0.1373. The structure was solved by direct methods and refined by full matrix least-squares on F^2, using SHELXTL 5.1 program packages. In refinements were used weights according to the scheme $w = [\sigma^2(F_o^2) + (0.0888P)^2 + 0.0000P]^{-1}$, where $P = (F_o^2) + 2F_c^2)/3$. The hydrogen atoms were located by geometrical calculations and refined using a "riding" method; wR_2 was equal to 0.1464. The goodness of fit parameter S was 0.909. The largest difference between peak and hole was 0.250 and −0.232 eÅ^{-3}. Crystallographic data (excluding structure factors and including selected torsion angles) have been deposited with the Cambridge Crystallographic Data Center, CCDC number 198754.

HPLC Separation. HPLC separation of the atropisomers of **3** was performed at +20 °C on a Chiralcel OD-H column (5μm), 250 mm × 4.6 mm i.d., UV = 254 nm, flow rate = 0.5 mL/min (60:40 hexane/^{i}Pr$_2$O). The necessary amount of the two separated enantiomers was obtained by collecting several elutions (100 μL of a 1.25 mg/mL solution each one).

CD Spectra of 3. CD spectra of **3** were recorded at +25 °C on a Jasco J-600 dicrograph in a 0.01 cm cell in the range 190−325 nm. Detailed spectra of the 260−325 nm region were obtained using a 0.1 cm cell. The concentration was 0.45 mg/mL (1.26 × 10^{-3} M in n-hexane). An ϵ = 89.200 was observed at 225 nm in the UV spectrum.

NMR Measurements. ^{13}C NMR spectra were recorded at 75.5 MHz, and the signal assignments were supported by DEPT and two-dimensional experiments.[9] The spectra at low temperatures were obtained by cooling the sample by a flow of dry nitrogen passing in an exchanger immersed in a bucket of liquid nitrogen. The temperature was calibrated before the VT experiments by means of a thermocouple, which has an uncertainity not exceeding ±1 °C. The line shape computer simulations were performed by a computer program based on DNMR6 routines,[22] and the best fit was visually judged by overlapping the experimental and calculated traces. The intrinsic line width was measured from the spectra taken at temperatures where the motion is "frozen". We also checked that an uncertainty on such a width as large as ±50% affected the rate constants by less than ±15% and, hence, the $\Delta G^{\ddagger}$ by ±0.05 kcal/mol: this corresponds to the error when two $\Delta G^{\ddagger}$ values are obtained at exactly the same temperature within the same sample. On the other hand, when the combined errors on the line width and on the temperature have to be taken into account, the uncertainty on the absolute value of $\Delta G^{\ddagger}$ becomes ±0.15 kcal/mol. The samples for measurements below −100 °C were prepared by connecting the NMR tubes, containing a small amount of a deuterated compound for a locking purpose, to a vacuum line and condensing the gaseous solvents ($CHFCl_2$ and CHF_2Cl) with liquid nitrogen. The tubes were then sealed in vacuo and introduced into the precooled probe of the spectrometer.

Acknowledgment. A research fund for young researchers from the University of Bologna is acknowledged by S.G. Financial support from the University of Bologna (Funds for selected research topics 2001−2002) and from MIUR-COFIN 2001, Rome (national project "Stereoselection in Organic Synthesis"), was received by L.L. and A.M. Support from the University of Basilicata and from MIUR-COFIN 2001, Rome ("New theoretical and experimental methods for the assignment of the molecular configuration in solution"), was also received by D.C. and C.R. The authors thank Prof. P. Righi, Department of Organic Chemistry, University of Bologna, for helping with enantioselective HPLC separation.

JO0265378

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