Correct Values of the Rotation Barriers of 1,8-Ditolylanthracenes

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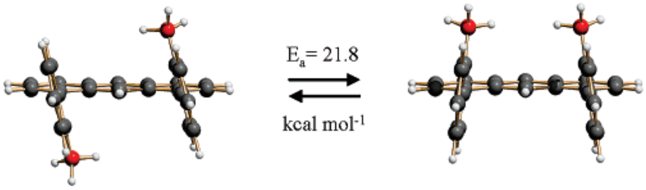


The rotation barriers of two 1,8-ditolylanthracene derivatives have been measured by accurate line-shape simulation of their variable-temperature NMR spectra. Both values were found to be more than twice as large as those previously reported in the literature.

Some time ago House and co-workers[2] measured, by variable-temperature NMR spectroscopy, the rotation barriers of 1,8-diarylanthracene derivatives. The values, reported as activation energies derived from the Arrhenius equation, were unusually low with respect to the expectation for this type of compound, e.g., 5.3 and 10.4 kcal mol^{-1} for compounds **1** and **2**, respectively (Chart 1). The authors themselves were surprised by such incredibly low values and a few years later published a paper[3] where a possible explanation was proposed.

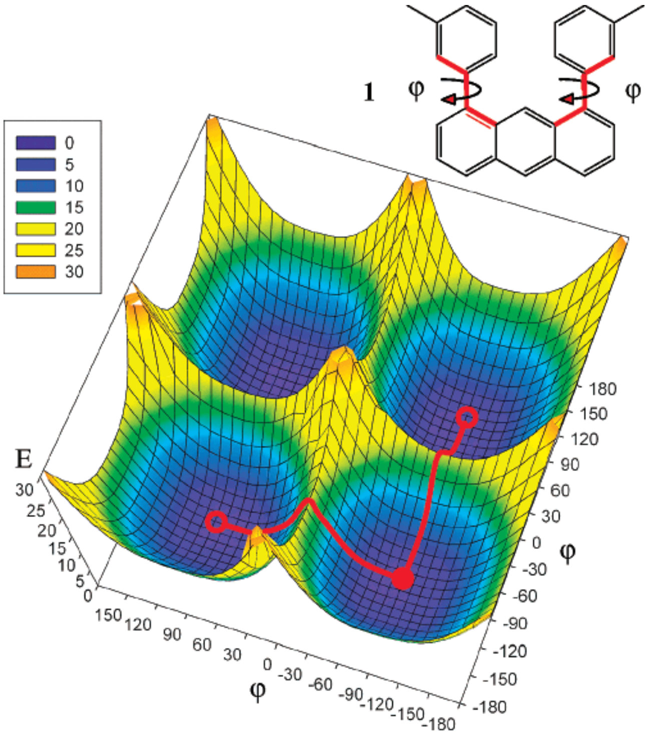
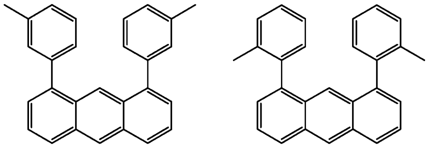


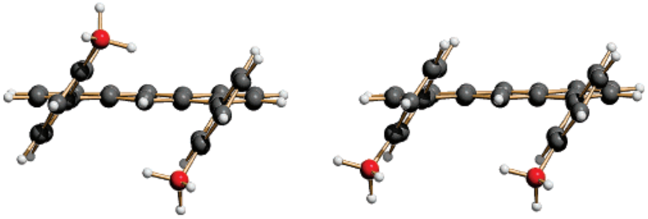
FIGURE 1. Energy surface (*E* in kcal mol^{-1}) and rotation pathways computed[4] as a function of the two torsion angles (φ) about the tolyl–anthracene bonds of derivative **1**. The solid and open dots represent the trans and cis conformer, respectively.

CHART 1



1 **2**

SCHEME 1. Ab Initio Computed Structures of the Trans and Cis Conformers of 1[a]



1-trans (E = 0.0) **1**-cis (E = 0.2)

[a] The relative energies (*E*) are in kcal mol^{-1}. Methyl groups are shown in red for convenience). The small amplitude torsion (libration) of the tolyl ring about the orthogonal situation has a very small barrier (less than 1 kcal mol^{-1}), so that in the NMR timescale the trans form displays dynamic C_2 (chiral) and the cis form dynamic C_s (achiral) symmetry.

The energy surface of compound **1**, computed[4] as a function of the anthracene–tolyl torsion angle φ (Figure 1), shows that the rotation pathways interconverting the trans and cis conformers (indicated by red lines) run parallel to the respective axes, indicating that the two motions are independent of each other and the processes, accordingly, are not correlated.[5] The rotation barrier is calculated to be much larger (about 16 kcal mol^{-1}) than the reported[2] value. Such a theoretical value was refined using the more reliable ab initio approach[6] that likewise indicated the trans form to be more stable than the cis form (by 0.2 kcal mol^{-1} as in Scheme 1) and predicted again the existence of a sp^2–sp^2 rotation barrier (12.2 kcal mol^{-1}) still significantly larger than the 5.3 kcal mol^{-1} value from the literature.[2] A similar value had been also calculated[7] (12.9 kcal mol^{-1}) for

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[1] In partial fulfillment for receiving a Ph.D. degree in Chemical Sciences, University of Bologna

[2] House, H. O.; Hrabie, J. A.; VanDerveer, D. *J. Org. Chem.* **1986**, *51*, 921.

[3] House, H. O.; Holt, J. T.; VanDerveer, D. *J. Org. Chem.* **1993**, *58*, 7516.

[4] Molecular Mechanics approach using the MMFF force field as in PC Model v 7.5, Serena Software, Bloomington, IN.

[5] (a) Casarini, D.; Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 2757. (b) Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 4444. (c) Grilli, S.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2001**, *66*, 5853. (d) Jog, P. V.; Brown, R. E.; Bates, D. K. *J. Org. Chem.* **2003**, *68*, 8240. (e) Casarini, D.; Lunazzi, L.; Mazzanti, A.; Mercandelli, P.; Sironi, A. *J. Org. Chem.* **2004**, *69*, 821.

[6] Frisch, M. J., et al. *Gaussian 03*, Revision D.01; Gaussian, Inc.: Wallingford, CT, 2004 (See Supporting Information).

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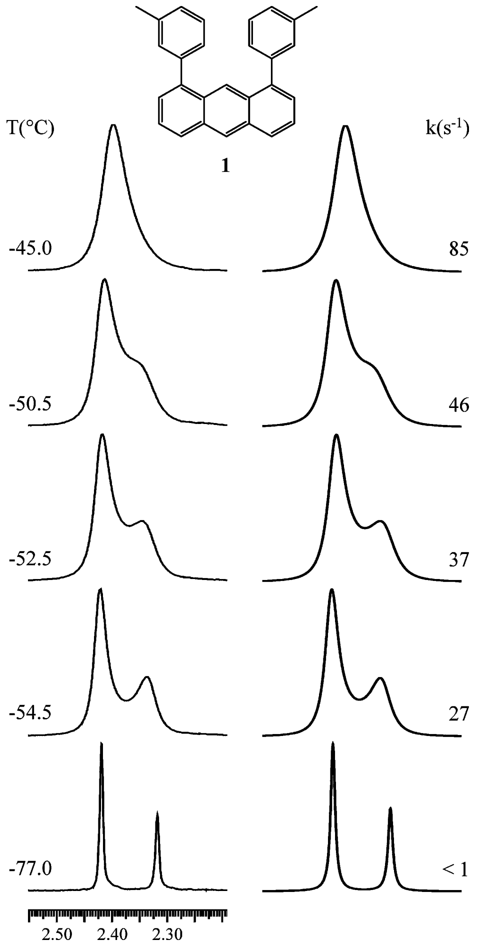

FIGURE 2. (Left) ^1H NMR methyl signals of compound **1** (600 MHz in CD_2Cl_2) as a function of temperature. (Right) Line-shape simulation obtained with the rate constants indicated.

the sp^2-sp^3 rotation barrier in an anthracene substituted by two CF_3CHOH groups in positions 1 and 8, although in that case an experimental determination to confirm the theoretical prediction had not been provided.

Also, the ab initio computed[6] barrier of **2** (20.8 kcal mol^{-1}) turned out to be much higher than 10.4 kcal mol^{-1}.[2,3] Since the values derived from these calculations are seemingly at variance with the experimental data, we performed an accurate verification of the previous experiments by taking advantage of better instrumentation than available in the past. Compounds **1** and **2** were selected for this purpose because determinations of the corresponding barriers could be carried out in both the low temperature (compound **1**) and the high-temperature (compound **2**) range.

As shown in Figure 2 (left) the ^1H NMR spectrum of **1** (600 MHz in CD_2Cl_2) at −77 °C displays two methyl signals with different intensities, the ratio being 63:37. The more intense downfield signal was assigned to the chiral trans conformer, following the prediction of the above-mentioned ab initio computations (Scheme 1).

The computer line-shape simulation[8] of these lines was performed at 10 significant temperatures in the range −66 to −45 °C: a few selected sample traces are reported in Figure 2 (right). Also, the aromatic hydrogen in position 9 yields two signals with the same 63:37 ratio, and these were likewise simulated at the same temperatures where the methyl lines had been examined. Equal values for the rate constants were obtained in both cases, thus providing an independent check of the accuracy of the present data. The 10 rate constants obtained in this way (Table S-1 of Supporting Information) allowed us to derive the activation parameters using both the Eyring and the Arrhenius equations. The corresponding data are collected in Table 1, and as often observed in the dynamics of conformational processes, the $\Delta S^\ddagger$ value is negligible[9] within the experimental uncertainty. From our experiment it is quite evident that the interconversion barrier, indicated either as $\Delta G^\ddagger$, $\Delta H^\ddagger$, or E_a, is in good agreement with the ab initio calculations[10] but more than twice as large as the 5.3 kcal mol^{-1} value of the previous experiments.[2]

TABLE 1. Experimental Activation Parameters for Compounds 1 and 2 ($\Delta G^\ddagger$, $\Delta H^\ddagger$, E_a in kcal mol^{-1}, $\Delta S^\ddagger$ in cal mol^{-1} T^{-1})[a]

compound	$\Delta G^\ddagger$	$\Delta H^\ddagger$	$\Delta S^\ddagger$	E_a	log *A*
1	11.22 (0.02)	11.45 (0.2)	1.1 (1.0)	11.9 (0.2)	13.3 (0.2)
2	21.30 (0.03)	21.0 (0.3)	−0.75 (1.0)	21.8 (0.3)	13.2 (0.2)

[a] The value in parentheses is the estimated uncertainty.

Distinguishable NMR methyl signals for the cis and trans conformers of **2** are observed at ambient temperature, the upfield signal displaying a slightly higher intensity, i.e., 54% in $CDCl_3$ and 53% in dimethylformamide-d_7 (DMF-d_7). Ab initio calculations[6] indicate that the cis form has an energy 0.25 kcal mol^{-1} higher than the trans form (Supporting Information), suggesting again that the latter should be the more stable conformer. It should be pointed out, however, that the relative proportions of the trans and cis conformers are nearly equal in this case, thus making an assignment based solely on theoretical considerations less reliable. For this reason we also obtained the support of an experimental determination.

Following the procedure reported[11] for the assignment of symmetric isomers, the ^{13}C satellite spectra of the methyl signals

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(7) Pérez-Trujillo, M.; Maestre, I.; Jaime, C.; Alvarez-Larena, A.; Pinella, J. F.; Virgili, A. *Tetrahedron: Asymmetry* **2005**, *16*, 3084.

(8) PC version of the DNMR program no. 633, QCPE, Indiana University, Bloomington, IN.

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(10) Since the trans to cis conversion can be accomplished by rotation of either of the two tolyl rings, the rotation rate of a single ring corresponds to one-half of the measured rate constants. The corresponding $\Delta G^\ddagger$, $\Delta H^\ddagger$, and E_a thus become, in this case, 0.3 kcal mol^{-1} higher (i.e. 11.5, 11.8, and 12.2 kcal mol^{-1}, respectively), and it is these values that, in principle, should be compared to the theoretical rotation barrier of 12.2 kcal mol^{-1} (see Lunazzi, L.; Mazzanti, A.; Minzoni, M. *J. Org. Chem.* **2007**, *72*, 2501).

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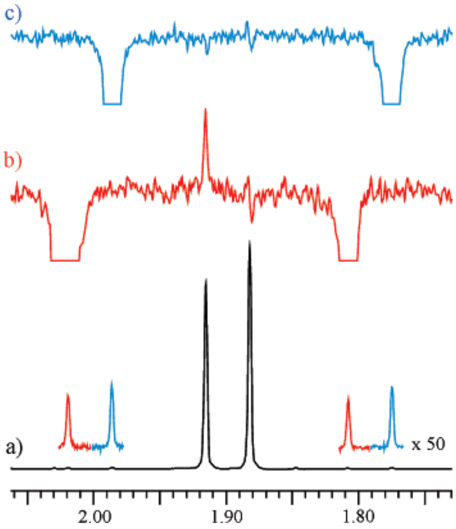

FIGURE 3. (a) Methyl signals (^{1}H, 600 MHz) of **2** in $CDCl_3$ at 0 °C[13] displaying in the inset the ^{13}C satellite signals. (b) Spectrum obtained by irradiating the satellites of the downfield line. (c) Spectrum obtained by irradiating the satellites of the upfield line.

of each of the two conformers were irradiated using the DPFGSE-NOE sequence.[12] As shown in Figure 3 (trace b), irradiation of the satellites of the less intense low-field signal yields a substantial NOE effect, indicating that this signal corresponds to the cis conformer, where the hydrogens of the two methyl groups are sufficiently close (computed average distance 4.60 Å) as to experience a reciprocal NOE enhancement. On the other hand, irradiation of the satellites of the more intense upfield signal (trace c) does not produce any NOE effect, indicating that this corresponds to the trans conformer, where the hydrogens of the two methyl groups are too far apart (computed average distance 6.94 Å) to experience the reciprocal NOE enhancement. These experimental results confirm, therefore, the theoretical assignment.

As shown in Figure 4 (left) the two methyl signals of **2** broaden on raising the temperature (in DMF-d_7 as solvent), eventually coalescing into a single line. Line-shape simulation (Figure 4, right) provides the corresponding rate constants for the trans to cis interconversion. Twelve such rates were determined in the range from 104 to 136 °C (Table S-2 of Supporting Information), and from these values the activation parameters collected in Table 1 were obtained.[14] In this case the experimental barrier also agrees well with that predicted by the ab initio computations and is at least twice as large as the 10.4 kcal mol^{-1} previously reported.[2,3]

It is therefore demonstrated that the unusually low values quoted for the barriers of **1** and **2** were the consequence of measurements of insufficient accuracy, so that it is not necessary to propose any explanation to justify barriers that actually are in keeping with the expectations. For instance, the barrier of **1** lies in the same range as that of biphenyls bearing a single substituent of analogous size in the ortho position[15] and that of **2** lies in the same range as that of biphenyls bearing two substituents of analogous size in the ortho, ortho′ positions.[16]

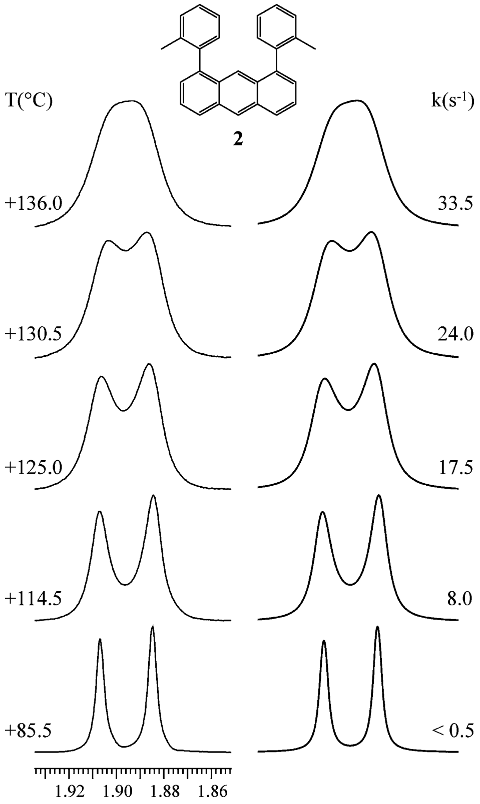

FIGURE 4. (Left) ^{1}H NMR methyl signals of compound **2** (600 MHz in DMF-d_7) as a function of temperature. (Right) Line-shape simulation obtained with the rate constants indicated.

Experimental Section

Materials. 1,8-Dibromoanthracene[7] was prepared according to the literature; *o*- and *m*-tolylboronic acids were commercially available as well as the $Pd(PPh_3)_4$ catalyst.

1,8-Di-*m*-tolylanthracene (1).[2] To a solution of 1,8-dibromoanthracene (0.336 g, 1 mmol in 6 mL of benzene), K_2CO_3 (2 M solution, 1.25 mL), *m*-tolylboronic acid (0.340 g, 2.5 mmol, suspension in 6 mL of ethanol), and $Pd(PPh_3)_4$ (0.231 g, 0.2 mmol) were added at room temperature. The stirred solution was refluxed for 2−3 h, the reaction being monitored by GC-MS. After the first coupling was complete, a second amount of *m*-tolylboronic acid (0.340 g, 2.5 mmol, suspension in 6 mL of ethanol) and $Pd(PPh_3)_4$ (0.231 g, 0.2 mmol) were added at room temperature, and the solution was refluxed again for 3 h. Then $CHCl_3$ and H_2O were added, and the extracted organic layer was dried (Na_2SO_4) and evaporated. The crude product was prepurified by chromatography on silica gel (hexane/Et_2O 50:1) to yield 0.28 g of a mixture containing mainly 1-bromo-8-*m*-tolylanthracene, 1-*m*-tolylanthracene, and compound **1**. Analytically pure samples of **1** were obtained by semipreparative HPLC on a Luna C18(2) column (5 μm, 250 × 10 mm, 4 mL/min, ACN/H_2O 90:10 v:v).

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[12] (a) Stonehouse, J.; Adell, P.; Keeler, J.; Shaka, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 6037. (b) Stott, K.; Stonehouse, J.; Keeler, J.; Hwang, T. L.; Shaka, A. J. *J. Am. Chem. Soc.* **1995**, *117*, 4199. (c) Stott, K.; Keeler, J.; Van, Q. N.; Shaka, A. J. *J. Magn. Reson.* **1997**, *125*, 302. (d) Van, Q. N.; Smith, E. M.; Shaka, A. J. *J. Magn. Reson.* **1999**, *141*, 191.

[13] The NOE experiment was carried out at 0 °C to avoid the possibility of a saturation transfer process between the two conformers.

[14] As discussed in ref 10, rotation of a single tolyl group of **2** has, in this case, an activation parameter 0.5 kcal mol^{-1} higher.

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[16] Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618.

1,8-Di-*o*-tolylanthracene (**2**)[2] was prepared using the same procedure of **1** and *o*-tolylboronic acid.

NMR Spectroscopy. The spectra were recorded at 600 MHz for ^{1}H and 150.8 MHz for ^{13}C. The assignments of the ^{13}C signals were obtained by two-dimensional experiments (edited-gHSQC[17] and gHMBC[18] sequences). Temperature calibrations were performed immediately before the experiments using a Cu/Ni thermocouple immersed in the same solvents used for the measurements (CH_2Cl_2 and DMF) contained in a nonspinning dummy sample tube and under conditions as nearly identical as possible. The uncertainty in the temperatures was estimated from the calibration curve to be ±0.5 °C. Line-shape simulations[8] were performed by taking into account the chemical shift variation as a function of temperature: shifts were measured below the exchange region and extrapolated into the temperature range where simulations were performed. The monodimensional NOE experiments of **2** were obtained in $CDCl_3$ at 0 °C[13] by means of the DPFGSE-NOE[12] sequence. To selectively irradiate the two ^{13}C satellites, a double-frequency[19] 10 Hz wide shaped pulse was calculated with a refocusing-SNOB shape[20] and a pulse width of 185 ms.

Calculations. Computations were carried out at the B3LYP/6-31G(d) level by means of the Gaussian 03 series of programs[6] (see Supporting Information): the standard Berny algorithm in redundant internal coordinates and default criteria of convergence were employed. The reported energy values are not ZPE corrected. Harmonic vibrational frequencies were calculated for all the stationary points. For each optimized ground state the frequency analysis showed the absence of imaginary frequencies, whereas each transition state showed a single imaginary frequency. Visual inspection of the corresponding normal mode was used to confirm that the right transition state had been found.

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Supporting Information Available: Calculated structures of conformers of **2**, tables of rate constants, ^{1}H and ^{13}C NMR results, HPLC traces, and computational data for compounds **1**−**2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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