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Stereodynamics of 1-*tert*-Butyl-8-fluoronaphthalene. Restricted *tert*-Butyl Rotation about an sp^3–sp^2 Carbon–Carbon Bond. An Unusually High Barrier to Isolated Methyl Rotation. Through-Space Spin–Spin Coupling to Fluorine

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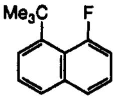
When considering the stereodynamics of organic molecules, rotation about carbon–carbon single bonds is a fundamentally important rate process.[1a] It is now well-established that, in addition to molecular orbital control, nonbonded repulsions play important roles in determining internal rotation barriers and molecular conformational preference. There are relatively few examples of dynamic NMR (DNMR) studies of *tert*-butyl rotation about an sp^3–sp^2 carbon–carbon bond.[1a] An important case in which nonbonded repulsions can play a dominant role is the interaction between peri substituents on the naphthalene ring.[1b] In studying the consequences of such nonbonded repulsions, 1-*tert*-butyl-8-fluoronaphthalene (**BFN**) is a representative compound. This paper reports the results of ^{13}C and ^{1}H DNMR studies of **BFN** complemented by molecular mechanics calculations that reveal a strongly preferred C_s-symmetric equilibrium conformation that has one methyl carbon coplanar with the naphthalene ring and proximate to C2 of the ring. Decoalescence of the DNMR spectra reveals both restricted *tert*-butyl rotation and an unusually high barrier to isolated rotation of the methyl group that eclipses the ring. The DNMR spectra at slow exchange also demonstrate the distance dependence of through-space spin–spin coupling of ^{13}C or ^{1}H to ^{19}F in a conformationally flexible molecule.



BFN

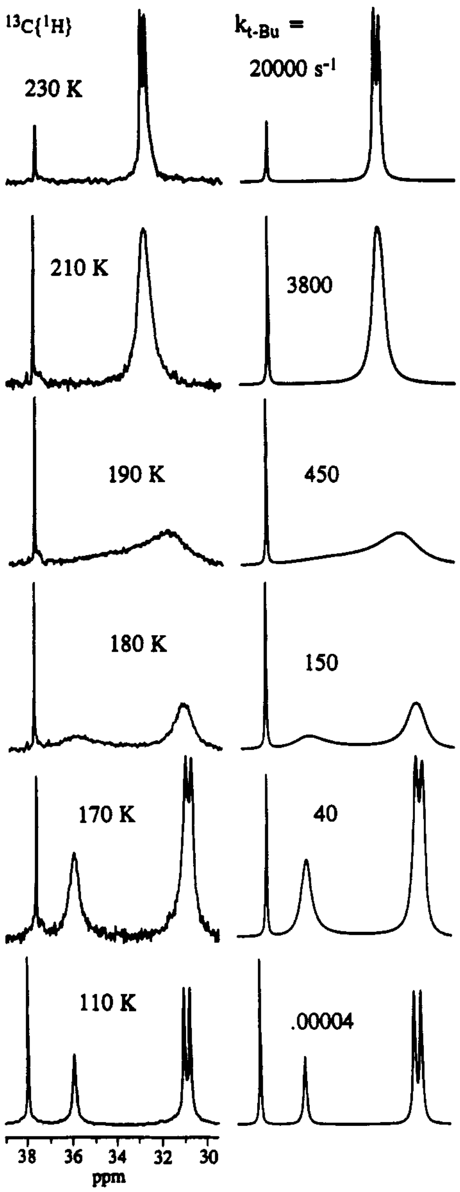


Figure 1. The experimental ^{13}C DNMR spectra (62.898 MHz) of the *tert*-butyl group of 1-*tert*-butyl-8-fluoronaphthalene (5% v/v in $CBrF_3$) in the left column and theoretical simulations in the right column calculated as a function of the rate of *tert*-butyl rotation.

The ^{13}C NMR spectrum (62.9 MHz) of **BFN** (5% v/v in $CBrF_3$) at 230 K shows a doublet resonance at δ 32.9 (J_{CF} = 12 Hz; methyl carbons) and a singlet at δ 37.8 (*tert*-butyl quaternary carbon) consistent with rapid conformational interconversion on the NMR chemical exchange time scale (Figure 1). At lower temperatures, the signal due to the methyl carbons decoalesces asymmetrically and, at 110 K, is sharpened into a broad singlet at δ_A 35.9 and a doublet at δ_B 30.8 (J_{CF} = 19 Hz). Because isolated methyl rotation is invisible to the ^{13}C DNMR method, the DNMR behavior shown in Figure 1 must be assigned to slowing *tert*-butyl rotation. The DNMR spectra shown in Figure 1 were simulated by using an exchange of magnetization among the A, B, and B frequencies of one AX (X = ^{19}F, $J_{AX} \approx 0$ Hz) and two BX (J_{BX} = 19 Hz) spin systems.[2] The rate constants in Figure 1 correspond to conversion of one *tert*-butyl rotamer to one other rotamer. From the rate constants determined from the simulations at various temperatures, the activation parameters for *tert*-butyl rotation can be calculated ($\Delta H^* = 8.3 \pm 0.4$ kcal/mol; $\Delta S^* = -2 \pm 4$ cal/mol-K; $\Delta G^* = 8.6 \pm 0.1$ kcal/mol at 180 K).

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(1) (a) Oki, M. *Applications of Dynamic NMR Spectroscopy to Organic Chemistry*; VCH: Deerfield Beach, 1985. Orville-Thomas, W.J., Ed. *Internal Rotation in Molecules*; J. Wiley and Sons: New York, 1974. (b) Anderson, J. E.; Cooksey, C. J. *Chem. Commun.* 1975, 942 and references cited therein.

(2) The computer program used to simulate the DNMR spectra is DNMR4 (Bushweller, C. H.; Letendre, L. J.; Brunelle, J. A.; Bilofsky, H. S.; Whalon, M. R.; Fleischman, S. H. *QCPE* 1983, program no. 466). DNMR4 has been modified to operate in the VMS VAX Fortran 77 format.

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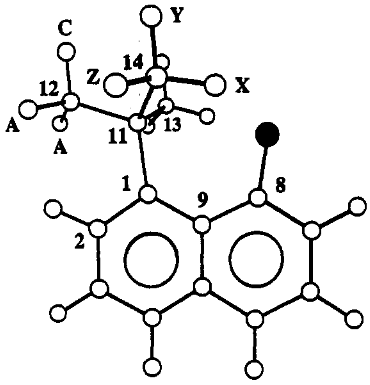
The spectrum at 110 K is consistent with a molecular conformation that has C_s symmetry. Two of the methyl carbons are either homotopic or enantiotopic and give the doublet at δ_B 30.8. The singlet at δ_A 35.9 is due to a unique methyl carbon that must lie in the plane of the naphthalene ring. Two diastereomeric conformations have geometries that are consistent with the 110 K spectrum. One conformation has the unique methyl carbon next to and coplanar with C2 of the naphthalene ring and the other two methyl carbons flanking the fluorine (**1**). The other conformation has the unique methyl carbon proximate to fluorine and coplanar with the naphthalene ring while the other two methyl carbons flank the proton on C2 (**2**). An examination of a model of **2** suggests serious nonbonded repulsions between the unique methyl group and fluorine and suggests strongly that **2** is substantially less stable than **1**. Molecular mechanics calculations done by using Allinger's MM2 (87) force field predict that **1** is the most stable equilibrium conformation and is 5.6 kcal/mol more stable than **2**.[3] In **1**, the MM2-calculated C9–C1–C11–C12 dihedral angle is 180°. An MM2 (87) general dihedral angle driver calculation for *tert*-butyl rotation indicates that **2** is a *highly unstable intermediate* along the energy profile for rotation. The energy profile generated from this dihedral angle driver calculation is illustrated in Figure 2. Starting from **1**, a 48° rotation of the *tert*-butyl group produces the transition state (dihedral angle C9–C1–C11–C12 = 228°). The MM2-calculated barrier to rotation is 5.7 kcal/mol. This calculated barrier is 2.6 kcal/mol lower than the DNMR value. An additional 12° torsion produces a shallow energy minimum that corresponds to **2** (dihedral angle C9–C1–C11–C12 = 240°) which is calculated to be only 0.1 kcal/mol lower in energy than the transition state. The calculations suggest that there is a gearing of the methyl group as it passes the fluorine during *tert*-butyl rotation.



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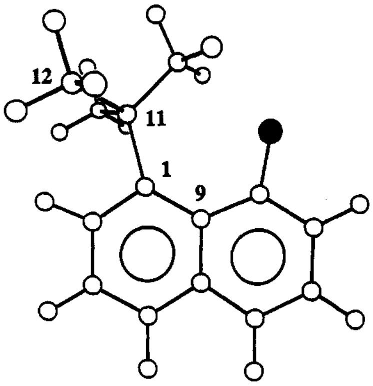
● **F**



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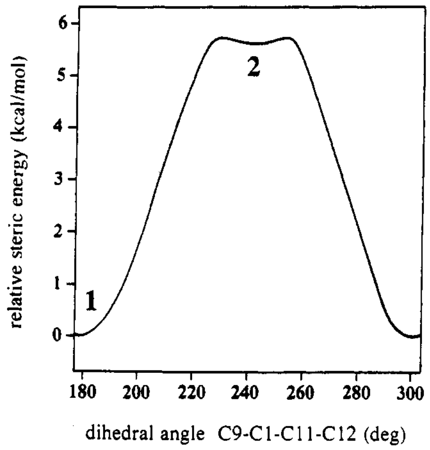

Figure 2. The energy profile for *tert*-butyl rotation in 1-*tert*-butyl-8-fluoronaphthalene calculated by using the general dihedral angle driver option in Allinger's MM2(87) molecular mechanics force field.[3]

The 110 K spectrum provides a dramatic illustration of the distance dependence of "through-space", electron-pair mediated spin–spin coupling.[4] In light of the fact that the methyl carbons are separated from fluorine by five bonds, the observed coupling does not occur predominantly through bonds but does occur mainly through space. The ^{13}C resonance at δ_B 30.8 shows a dramatically larger coupling of ^{13}C to ^{19}F than the signal at δ_A 35.9. Based on the time-averaged J_{CF} value of 12 Hz observed at 230 K, the 19-Hz coupling associated with the dominant doublet observed at 110 K implies a −2-Hz coupling to the unique carbon. While the resonance at δ_A 35.9 is differentially broadened, no splitting is observed. This apparent discrepancy could be due to a temperature dependence of the large coupling constant and/or different T_2 values for the two methyl signals. The generally broad lines at 110 K could easily obscure a −2-Hz coupling. It is simply not possible to determine unequivocally the extent of coupling of the remote carbon to fluorine. The larger coupling associated with the resonance at δ_B 30.8 is consistent with the fact that the two carbons that give this signal (C13 and C14; see structure **1**) are much closer to fluorine than C12. The MM2-calculated interatomic distance between C13 or C14 and fluorine is 2.82 Å. The distance between C12 and fluorine is 4.41 Å.

The ^1H DNMR spectra (250 MHz) of **BFN** (5% v/v in $CBrF_3$) revealed additional interesting aspects of the stereodynamics. At 220 K, the spectrum shows one sharp doublet at δ 1.59 (J_{HF} = 2 Hz) revealing through-space

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[3] Allinger, N. L. *QCPE* **1987**, program no. MM2(87).

[4] Contreras, R. H.; Natiello, M. A.; Scuseria, G. E. *Magn. Reson. Rev.* **1985**, *9*, 239. Hilton, J.; Sutcliffe, L. H. *Prog. NMR Spectrosc.* **1975**, *10*, 27. Hsee, L. C.; Sardella, D. J. *Magn. Res. Chem.* **1990**, *28*, 688. Mallory, F. B.; Mallory, C. W.; Baker, M. B. *J. Am. Chem. Soc.* **1990**, *112*, 2577. Balonga, P. E.; Kowalewski, V. J.; Contreras, R. H. *Spectrochem. Acta, Part A* **1988**, *44A*, 819. Gribble, G. W.; Kelly, W. J. *Tetrahedron Lett.* **1985**, *26*, 3779. Barfield, M.; Walter, S. R.; Clark, K. A.; Gribble, G. W.; Haden, K. W.; Kelly, W. J.; LeHoullier, C. S. *Org. Magn. Res.* **1982**, *20*, 92.

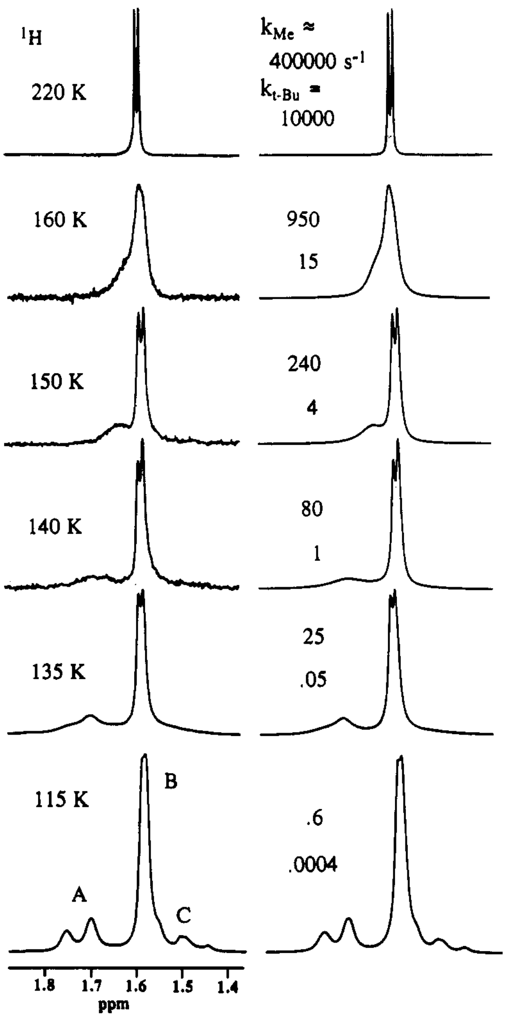

Figure 3. The experimental ^1H DNMR spectra (250.136 MHz) of the *tert*-butyl group of 1-*tert*-butyl-8-fluoronaphthalene (5% v/v in $CBrF_3$) in the left column and theoretical simulations in the right column calculated as a function of the rate of *tert*-butyl rotation ($k_{t\text{-Bu}}$) and methyl rotation (k_{Me}).

coupling of ^1H to ^{19}F and rapid conformational exchange. Once again, *through-bond* coupling of ^1H to ^{19}F would have to occur via six bonds and should be minuscule. At lower temperatures, the spectrum decoalesces in a distinctly asymmetric fashion (Figure 3). At 115 K, the spectrum is simulated accurately by the superposition of two subspectra. The major subspectrum is a T_2-broadened doublet at δ_B 1.58 (J_{HF} = 3 Hz). The minor subspectrum is simulated accurately as an A_2C spin system (δ_A 1.72, δ_C 1.50; J_{AC} = −13.5 Hz); no spin–spin coupling to ^{19}F is required. The area ratio of the major subspectrum to the minor subspectrum is 2:1. One is led inexorably to assign the major doublet to the enantiotopic C13 and C14 methyl groups in 1. The larger coupling associated with the dominant doublet is consistent with the smaller MM2-calculated interatomic distances between the fluorine and protons X (2.14 Å), Y (3.42 Å), and Z (3.67 Å) as compared to protons A (5.01 Å) and C (4.82 Å) in 1. The doublet reveals that isolated rotation of the C13 and C14 methyl groups is fast on the NMR chemical exchange time scale at 115 K. This is consistent with an MM2-calculated barrier equal to 1.3 kcal/mol. The A_2C subspectrum must be assigned to the C12 methyl. *The observation of distinctly different resonances at δ_A 1.72 (2 H) and δ_C 1.50 (1 H), and a typical geminal proton–proton coupling constant (−13.5 Hz), reveals unequivocally that isolated rotation of the C12 methyl group is slow on the NMR chemical exchange time scale at 115 K.* The A_2C subspectrum is rigorously consistent with the C_s symmetry of the equilibrium conformation 1. The two "A" protons are enantiotopic and can be reflected through the mirror plane (see 1). The unique "C" proton is coplanar with the ring and is located in the mirror plane.

The DNMR spectra in Figure 3 are simulated accurately by employing a mutual exchange of magnetization among the A, A, and C frequencies of the A_2C spectrum as well as exchange of A_2C magnetization with two B_3X (X = ^{19}F, J_{BX} = 3 Hz) resonances.[2] The first process corresponds to isolated C12 methyl rotation (k_{Me} in Figure 3) and the latter exchange to *tert*-butyl rotation ($k_{t\text{-Bu}}$). The rate of isolated methyl rotation is faster than that for *tert*-butyl rotation (Figure 3). The activation parameters for methyl rotation are $\Delta H^\ddagger$ = 6.7 ± 0.4 kcal/mol, $\Delta S^\ddagger$ = −1 ± 4 cal/mol-K, and $\Delta G^\ddagger$ = 6.9 ± 0.1 kcal/mol at 150 K. The rate constants for *tert*-butyl rotation at various temperatures correspond well to those derived from simulations of the ^{13}C DNMR spectra (Figure 1). The MM2-calculated barrier for C12 methyl rotation is 10.1 kcal/mol. While the MM2 barrier is clearly too high, the MM2 force field does predict that C12 methyl rotation will have a higher barrier than C13 or C14 methyl rotation.

This paper reports an example of DNMR-detected restricted rotation about an sp^3–sp^2 carbon–carbon bond[1a] and a more rare case of a barrier to isolated methyl rotation that is high enough to be DNMR-visible in a relatively unencumbered, conformationally flexible molecule.[1,5] It is apparent that nonbonded repulsions between methyl groups and fluorine force **BFN** into the C_s-symmetric equilibrium conformation 1 and force the C12 methyl group into very close proximity with the proton on C2 of the ring. The MM2 calculations indicate that the interatomic distance between either of the "A" protons on C12 and the proton on C2 in 1 is 2.20 Å which is well within twice the van der Waals radius (1.2 Å) of hydrogen. The C12 methyl is forced into a perfectly staggered orientation in a sterically crowded environment. This situation clearly leads to the unusually high methyl rotation barrier.

The ^{13}C DNMR study also provides a clear-cut demonstration of the distance dependence of through-space coupling in a conformationally mobile system. Since conformational exchange is very fast at room temperature, this dependence could not be demonstrated without slowing *tert*-butyl rotation on the DNMR time scale. The results reported herein are analogous to those observed for a structurally similar tetrafluoro polycyclic molecule.[6] In the C_s-symmetric equilibrium conformation (3), the two enantiotopic methyl groups flank the proximate fluorine in a manner strictly analogous to **BFN**. *tert*-Butyl rotation is slow on the NMR time scale at room temperature. The coupling between the protons on the enantiotopic methyl groups and fluorine (2.9 Hz) is remarkably similar to that observed for **BFN** (3 Hz) at 115 K.

We are continuing studies of **BFN** analogues with the intention of assessing the effect of other peri substituents

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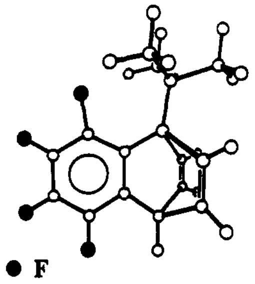
(5) Nakamura, M.; Oki, M.; Nakanishi, H. *J. Am. Chem. Soc.* **1973**, *95*, 7169. Nakamura, M.; Oki, M.; Nakanishi, H.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2415. Yamamoto, G; Oki, M. *Tetrahedron Lett.* **1985**, *26*, 457. Yamamoto, G; Oki, M. *J. Org. Chem.* **1984**, *49*, 1913. Anderson, J. E.; Rawson, D. I. *Chem. Commun.* **1973**, 830.

(6) Brewer, J. P. N.; Heaney, H.; Marples, B. A. *Chem. Commun.* **1967**, 27.



3

on barriers to rotation about carbon–carbon bonds in *tert*-butyl and other alkyl groups and also defining more quantitatively the distance dependence of through-space coupling in conformationally flexible systems.

Experimental Section

NMR Spectra. The NMR spectra were recorded by using a Bruker WM-250 NMR system equipped with an Aspect 3000 computer. The magnet pole gap has been modified to allow safe operation (no magnet O-ring freezing) down to temperatures as low as 93 K. NMR sample temperature was varied by using a custom-built cold nitrogen gas delivery system used in conjunction with the Bruker BVT-1000 temperature control unit. Temperature measurement is accurate to ±3 K. NMR samples were prepared in precision 5- or 10-mm tubes and sealed after four freeze–pump–thaw cycles. All spectra are referenced to tetramethylsilane at 0 ppm.

1-*tert*-Butyl-8-fluoronaphthalene (BFN). BFN was prepared as described previously.[7]

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(7) Gribble, G. W.; Keavy, D. J.; Olson, E. R.; Rae, I. D.; Staffa, A.; Herr, T. E.; Ferraro, M. B.; Contreras, R. H. *Magn. Res. Chem.* **1991**, *29*, 422.