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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 6199–6201

Stereodynamics of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane: experimental and theoretical analysis

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Received 21 April 2005; revised 28 June 2005; accepted 15 July 2005

Abstract—Dynamic NMR of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane reveals two dynamic processes: ring inversion leading to equilibrium between two degenerate rotamers of C_s symmetry ($\Delta G^{\neq} = 13.5$ kcal/mol), and rotation about the S–N bond leading to equilibrium between the C_s (more stable) and C_{3v} (2.12 kcal/mol less stable) rotamers ($\Delta G^{\neq} = 13.0$ kcal/mol).

Heterocyclohexanes, as well as cyclohexane itself, preferentially adopt the *chair* conformation[1] unless specific intramolecular interactions stabilize the more strained *twist* or *boat* conformers.[2] Substituents in the ring normally prefer equatorial over axial positions[1] though exceptions exist provided that 1,3-*syn* interactions with axial substituents are attractive (as in thiane *S*-oxides[3]) or absent (as in 1,3,5-trialkyl-1,3,5-triazinanes with two alkyls equatorial and third one axial[4,5]).

When studying the cascade transformations of trifluoromethanesulfonamide under the action of formaldehyde, we found 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane **1** among the products,[6] which showed interesting stereodynamic behavior in the ^{1}H, ^{13}C, and ^{19}F NMR spectra. The ^{1}H NMR spectrum of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane **1** in acetonitrile at room and at higher temperatures showed a broadened singlet resonance at 5.35 ppm due to the methylene protons. On cooling, it decoalesced at 15 °C into two signals of equal intensity, and at −15 °C these signals decoalesced further (Fig. 1a). Similar behavior was observed in methanol and acetone (Fig. 1b and c, respectively).

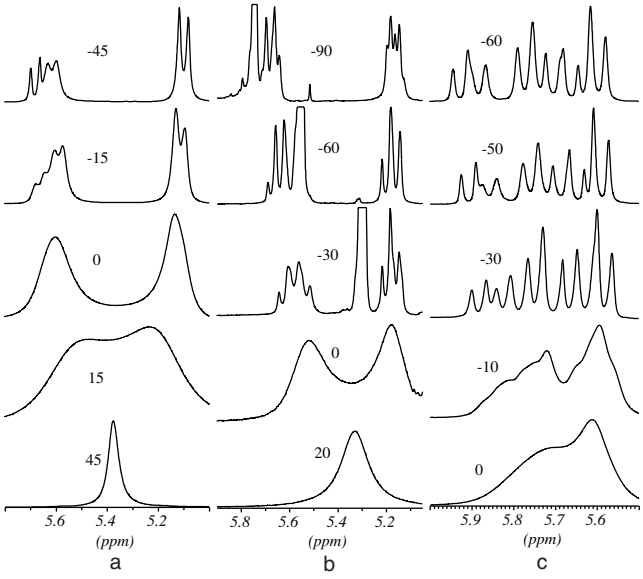

Figure 1. Temperature dependence (°C) of the ^{1}H NMR spectra of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane in CD_3CN (left), CH_3OH (figure), and $(CD_3)_2CO$ (right).

Therefore, compound **1** demonstrates two dynamic processes. The first one is ring inversion, while the second

Keywords: Conformational analysis; Tris(triflyl) substituted *symm*-triazinane; Dynamic NMR; Density functional calculations.
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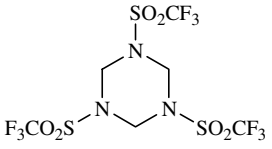
doi:10.1016/j.tetlet.2005.07.068



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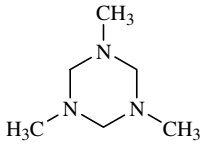

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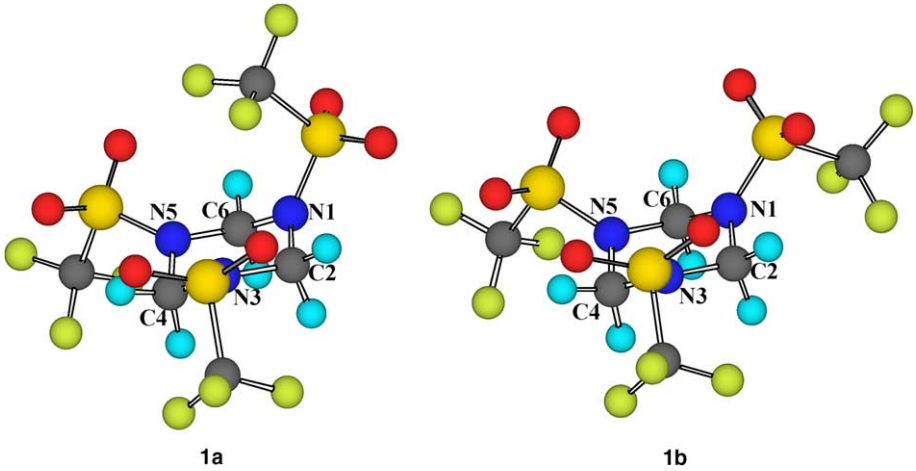
one, by analogy with 1,3,5-trialkyl-1,3,5-triazinanes,[4,5] could be inversion at the nitrogen atom provided that the latter is pyramidal. However, as shown by NMR and X-ray studies[7] the nitrogen atom in arenesulfonamides and more so in perfluoroalkanesulfonamides is planar rather than pyramidal. To clarify this problem, we applied density functional analysis[8] and optimized the geometry of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane **1** and, as a model compound, 1,3,5-trimethyl-1,3,5-triazinane **2**, whose stereodynamics were recently thoroughly studied.[4] The B3LYP/6-311G(d,p) calculations revealed two conformational minima on the potential energy surface of **1**. The lower lying minimum has C_s symmetry with one CF_3 group (belonging to substituent at N1) directed 'inward' (Fig. 2, **1a**). The second minimum is 2.12 kcal/mol higher and has C_{3v} symmetry with all three triflyl groups identical and directed 'outward' from the ring (Fig. 2, **1b**). Although formally an energy difference of $\geqslant$2 kcal/mol must virtually rule out **1b** from equilibrium at low temperatures, in solution the energy gap should be substantially lower due to the different polarity of conformers **1a** and **1b**: the dipole moment for the more stable conformer **1a** (6.13 D) is perceptibly lower than that for **1b** (7.98 D).

The model compound **2** has all the nitrogen atoms sp^3-hybridized forming normal pyramids with the sum of the bond angles around nitrogen equal to 335°, unlike the nitrogen atoms in compound **1**, which are virtually planar. The sum of the bond angles around nitrogen is 357.6° (N1) and 359.2° (N3, N5) for **1a**, and 359.8° for **1b**.

Therefore, no inversion at nitrogen can occur in compound **1** and one has to look for another possible dynamic process, which could be frozen in the NMR time scale. Since the triflyl group is not a symmetric rotor the only possibility remaining for the second dynamic process is internal rotation about the N–S bond.

The ^{1}H NMR spectrum of compound **1** in acetonitrile at −45 °C shows three doublets at δ 5.68 ppm (1H, J 14.1 Hz), 5.61 ppm (2H, broadened, J 13.0 Hz), and 5.10 ppm (3H, J 14.1 Hz) (Fig. 1a). The downfield doublet at 5.68 ppm belongs to H4-eq, the doublet at 5.61 to H2(6)-eq (its broadening can be explained on the assumption that in CD_3CN the rotation is not slow enough on the NMR time scale as well as by the long-range W-type coupling between H2 and H6), whereas all the axial methylene protons give one upfield doublet at 5.10 ppm. This assignment is in accordance with the ^{19}F NMR spectra of **1** in acetonitrile at −40 °C, which consists of one sharp singlet at −78.84 ppm belonging to the C_{3v} symmetrical rotamer and two broadened singlets at −78.44 and −75.84 ppm. The close values of the ^{19}F NMR chemical shifts for the first two singlets imply that they can be assigned to the triflyl groups oriented away from the ring in **1a** and **1b** whereas the signal at −75.84 ppm belongs to the triflyl group in **1a** directed 'inward' (Fig. 2). The relative intensity of the signals at −78.44 and −78.84 ppm (2:1) confirms this assignment.

Further decoalescence of the upfield signal of the axial protons is observed in methanol, where the room temperature singlet splits upon cooling into two multiplets of equal intensity (Fig. 1b). Under the conditions of restricted rotation the ^{1}H NMR spectrum of the mixture of rotamers **1a**+**1b** must show four lines due to H4-ax and H4-eq in **1a**, four lines due to H2(6)-ax and H2(6)-eq in **1a**, and four lines of H-ax and H-eq in **1b**. Indeed, the low-temperature spectrum in acetone (Fig. 1c) shows all 12 peaks (though some of them as partially resolved shoulders). In this spectrum, the two 'large' doublets at 5.61 and 5.78 ppm and one of the 'small' pairs of doublets at 5.70 and 5.86 ppm belong to unsymmetrical rotamer **1a**. The remaining two 'small' doublets at 5.92 and 5.66 ppm are ascribed to symmetrical rotamer **1b**.



1a 1b

Figure 2. The 'inward' (**1a**, C_s symmetry) and 'outward' (**1b**, C_{3v} symmetry) rotamers of 1,3,5-tris(trifluoromethylsulfonyl)-1,3,5-triazinane.

A common feature of the low-temperature spectra in all the solvents is relatively small chemical shift difference between the axial and equatorial protons in both **1a** and **1b** (0.5–0.6 ppm) and the very close values of the geminal coupling constants (13–14 Hz). The model compound **2** exhibits at 126 K (i.e., under the conditions of slow nitrogen inversion), two pairs of doublets, which are quite different regarding both chemical shift difference and spin–spin coupling (4H, $\Delta\delta$ 0.57 ppm, ^2J −11.2 Hz and 2H, $\Delta\delta$ 1.51 ppm, ^2J −7.9 Hz).[4] Such different behavior of compounds **1** and **2** definitely rules out any possibility of nitrogen inversion in **1**.

The ^{13}C NMR spectrum of compound **1** in acetonitrile contains one singlet due to methylene protons at 61.98 ppm and one CF_3 quartet at 120.34 ppm (J 320.4 Hz). On cooling both signals decoalesce and at −45 °C give two singlets at 61.51 (major) and 61.07 (minor), and two quartets at 119.26 ppm (J 319.4 Hz, major) and 119.52 ppm (J 321.5 Hz, minor). The ^{13}C NMR spectrum of **1** in acetone at −60 °C shows three magnetically non-equivalent methylene groups at 61.16, 61.55, and 61.68 ppm, as well as three quartets of the CF_3 groups at 119.29, 119.36, and 119.55 ppm.

The estimation of the energy of activation for both dynamic processes at the coalescence temperatures was carried out for the acetonitrile solution. The ring inversion has $\Delta G^{\neq} = 13.5$ kcal/mol at 290 K as determined from the ^{1}H NMR spectra. The restricted rotation of the triflyl group, as estimated from the temperature dependence of the ^{13}C NMR spectra, is characterized by $\Delta G^{\neq} = 13.0$ kcal/mol at 263 K. In a series of 1,3,5-trialkyl-1,3,5-triazinanes the trimethyl derivative has the largest barrier for cycle inversion, which amounts to 12.8 kcal/mol and this parameter decreases further to 11.4, 11.0, and 10.0 kcal/mol for the triethyl-, triisopropyl-, and tri-*tert*-butyl analogs, respectively.[4] Chair-to-chair inversion of **1a** or **1b** places two or three CF_3SO_2 groups in the 'inward' position, which is sterically impossible and compels them to turn away to the 'outward' position. Thus, it may be necessary for additional movement of atoms, which increases $\Delta G^{\neq}$ values for ring inversion in **1** in spite of the presence of planar segments, which is more usually known to decrease $\Delta G^{\neq}$ for ring inversion. The strong dependence of the signal shape on the temperature near the first (higher) coalescence point is indicative of a high positive activation entropy for cycle inversion.

Comparison of the measured barrier to triflyl group rotation for **1b** (13.0 kcal/mol) with the scarce literature data shows that it has an intermediate value between those for chlorosulfonamides $ClSO_2NR_2$ (11.0–11.4 kcal/mol)[9] and nonafluorobutane-1-sulfonamides $CF_3(CF_2)_3SO_2NR_2$ (14.9–16.7 kcal/mol).[7] This result can be rationalized in terms of the electron-withdrawing effect of trifluoromethyl group, which is more electronegative than that of chlorine but less electronegative than that of nonafluorobutyl group.[7]

^{1}H (400 MHz), ^{13}C (100 MHz), and ^{19}F (376 MHz) NMR spectra were recorded on a Bruker DPX 400 spectrometer; ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million downfield to TMS, and ^{19}F NMR in parts per million downfield to $CFCl_3$. The temperature was varied by the use of a BVT 3000 variable temperature unit, temperature stability ±0.2 °C.

Compound **1**: 6 g (0.04 mol) of $CF_3SO_2NH_2$ was dissolved in 100 mL of concd H_2SO_4 at 40 °C and 0.9 g (0.03 mol) of $(CH_2O)_n$ was added in small portions. The resulting thickened mixture was heated to 60–70 °C and stirred for 1 h. After cooling the mixture was poured into ice water, the precipitate filtered, washed with water and $NaHCO_3$, dried, and treated with hexane/ether (3:1). The insoluble material was dried and crystallized from isopropanol/hexane (1:1) to give 1.3 g (2.7 mmol, 27%) of **1**. Mp 217–218 °C. Elemental analysis: calcd for $C_6H_6F_9N_3O_6S_3$ (%): C 14.91, H 1.25, F 35.38, N 8.69, S 19.90; found: C 14.97, H 1.40, F 36.17, N 8.79, S 19.50.

References and notes

1. Bushweller, C. H. In *Conformational Behavior of Six-Membered Rings. Analysis, Dynamics, and Stereoelectronic Effects*; Juaristi, E., Ed.; VCH: New York, 1995.
2. Freeman, F.; Asgari, N.; Entezam, B.; Gomarooni, F.; Mac, J.; Nguyen, M. H.; Nguyen, N. N. T.; Nguyen, T. P.; Pham, N. B.; Sultana, P.; Welch, T. S.; Shainyan, B. A. *Int. J. Quant. Chem.* **2005**, *101*, 40–54.
3. Shainyan, B. A.; Kirpichenko, S. V. *Russ. J. Gen. Chem. (Engl. Transl.)* **2003**, *73*, 1709–1714.
4. Jewett, J. G.; Breeyear, J. J.; Brown, J. H.; Bushweller, C. H. *J. Am. Chem. Soc.* **2000**, *123*, 308–323.
5. Anderson, J. E.; Casarini, D.; Ijeh, A. I.; Lunazzi, L.; Tocher, D. A. *J. Am. Chem. Soc.* **1995**, *117*, 3054–3056.
6. Mescheryakov, V. I.; Albanov, A. I.; Shainyan, B. A. *Russ. J. Org. Chem. (Engl. Transl.)* **2005**, *41*, in press.
7. Lyapkalo, I. M.; Reissig, H.-U.; Schäefer, A.; Wagner, A. *Helv. Chim. Acta* **2002**, *85*, 4206, and references cited herein.
8. All calculations were performed at the B3LYP/6-31(d,p) level using the Gaussian98 program package: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M. Replogle, E. S.; Pople, J. A. GAUSSIAN 98, Revision A.6. Pittsburgh PA: Gaussian Inc., 1998.
9. Jennings, W. B.; Stratt, R. *J. Chem. Soc., Chem. Commun.* **1970**, 1418.