Structure and Stereodynamics of *N*-Methyl-*N*-9-triptycylacetamide: Pyramidal Amide Nitrogen in the Crystalline State

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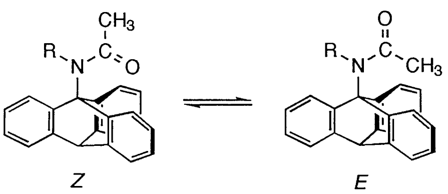
(Received March 25, 1997; CL-970214)

N-Methyl-*N*-9-triptycylacetamide exists as the *Z*-isomer in the crystalline state and the amide nitrogen is considerably pyramidal, while in solution the compound exists as a mixture of *E*/*Z* isomers, the equilibrium being dependent on the solvent and the temperature.

The cis-trans isomerism of amides and energy barriers to rotation about the amide bonds have long been the subjects of intense investigation.[1] Recently theoretical investigations on the nature of amide bonds have been made.[2]

We have been interested in the stereodynamics of various derivatives of 9-triptycylamine.[3,4] Recently we set in the studies on the stereodynamics of *N*-9-triptycylacetamide derivatives, where the effect of the bulky 9-triptycyl (Tp) group on the cis-trans isomerism and on the rotational barrier of the amide bond is of interest as well as the stereodynamics about the Tp–N bond.

In this communication, we report the molecular structures of *N*-9-triptycylacetamide (**1**) and its *N*-methyl derivative **2** in the crystalline state and the stereodynamics in solution studied by dynamic NMR spectroscopy.



1: R=H
2: R=CH_3

Compounds **1** and **2** were synthesized by acetylation with acetyl chloride of 9-triptycylamine[3b] and *N*-methyl-9-triptycylamine[3b] in the yields of 41 and 37%, respectively.[5]

X-ray crystallographic analysis of **1** and **2** revealed that both compounds exist as the *Z*-isomer in the crystalline state.[6]

Compound **1** adopts a near C_s geometry with the acetyl group bisecting two *o*-benzeno groups of the Tp moiety (Figure 1). The nitrogen atom may be assumed planar, though the position of the N-H hydrogen is not precisely determined.

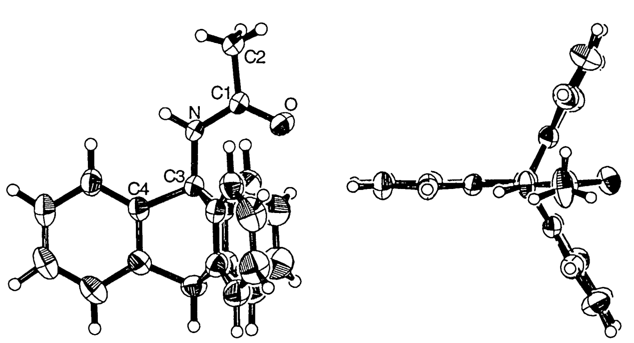


Figure 1. Side and top views of the molecular structure of **1**. Selected bond lengths (Å) and angles (°): C1-N, 1.352(2); C1-C2, 1.496(2); C1-O, 1.230(2); N-C3, 1.450(2); C1-N-C3, 122.6(1); N-C3-C4, 114.0(1); C1-N-C3-C4, 180.0; C2-C1-N-C3, –177.7; O-C1-N-C3, 2.5.

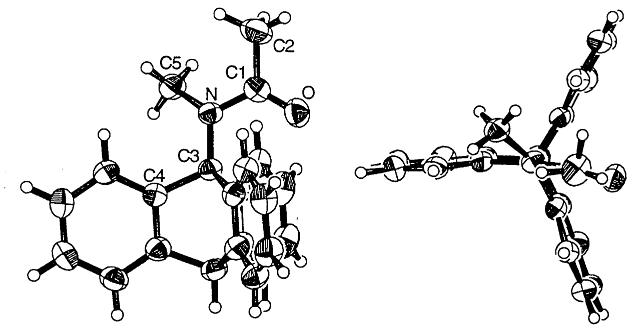


Figure 2. Side and top views of the molecular structure of **2**. Selected bond lengths (Å) and angles (°): C1-N, 1.383(3); C1-O, 1.218(3); C1-C2, 1.513(4); N-C3, 1.465(3), C1-N-C3, 119.0(2); C1-N-C5, 115.9(2); C3-N-C5, 117.0(2); N-C3-C4, 116.0(2); C1-N-C3-C4, 165.9; C5-N-C3-C4, -46.6; C2-C1-N-C3, -178.7; O-C1-N-C3, -0.6; C2-C1-N-C5, 33.4; O-C1-N-C5, -148.4.

For compound **2** two independent molecules are present in a crystal. As no significant difference in geometry is observed between the two, the drawing of one of them is given in Figure 2. The most significant feature is that the nitrogen is considerably pyramidalized, the sum of the three bond angles around the nitrogen being 351.9° for both of the independent molecules. Pyramidalization of an amide nitrogen atom seems unprecedented unless the nitrogen atom is incorporated in a cyclic structure.[7]

Steric effect might be responsible for the pyramidalization. As the bulky acetyl group tends to adopt a conformation bisecting the two *o*-benzeno groups, the *N*-methyl group should eclipse the third *o*-benzeno group if the nitrogen is planar. To avoid this eclipsing interaction, the nitrogen should pyramidalize.[8]

Differences in the geometrical parameters between **1** and **2** might be mainly ascribed to steric effects, although some features such as elongation of the amide C–N bond and slight shortening of the C=O bond upon going from **1** to **2** might partly be due to the change in the electronic structure.

Compound **1** is shown to exist as a single isomer in $CDCl_3$ and CD_2Cl_2. The well-established fact that secondary acetamides exist solely as the Z-isomer[1] together with the appearance of the acetyl protons of **1** at δ 2.52 in $CDCl_3$ (see below for **2**) unambiguously suggests that **1** exists solely as the Z-isomer in solution.

Compound **2** exists as a mixture of two isomers about the amide bond, *E* and *Z*, in solution. The isomer interconversion takes place slowly on the NMR timescale at 23 °C, and the NMR signals are slightly broadened. The isomer assignment is made from the chemical shifts of the acetyl protons: the Z-isomer gives the signal at δ 2.59 in $CDCl_3$ at 23 °C, while the *E*-isomer at a

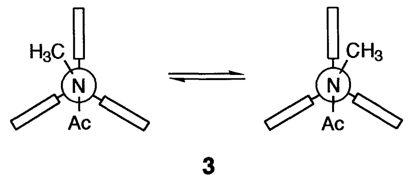
Table 1. Thermodynamic Parameters for the $Z \rightleftharpoons E$ Equilibrium in Compound **2**

Solvent	ΔH kJ mol^{-1}	ΔS J mol^{-1} K^{-1}	ΔG_{300K} kJ mol^{-1}	%Z(Temp/K)
$C_6D_5CD_3$	5.2±0.3	7.1±1.0	2.9_7	78 (300) 84 (250)
$CDCl_3$	6.0±0.5	8.9±1.7	3.3_3	79 (300) 86 (250)
CD_2Cl_2	9.4±0.4	9.4±1.4	6.6_0	93 (300) 97 (250)
$(CD_3)_2CO$				97.5 (250)

higher field of δ 1.72 due to the ring-current effect of the nearby *o*-benzeno rings. The isomer ratio depends significantly on solvent and temperature, though the *Z*-isomer is always more populated as expected from the steric effects among the groups. In $CDCl_3$ the *Z*/*E* ratio is 4.0 at 23 °C and 7.5 at −36 °C affording the thermodynamic parameters in Table 1. A very similar isomer distribution behavior is observed in toluene-d_8. In CD_2Cl_2 the population of the Z-isomer increases and the *Z*/*E* ratio is 14.5 at 23 °C and 38 at −36 °C. In acetone-d_6 the isomer equilibrium is even one-sided to the *Z*-isomer so that the thermodynamic parameters are not obtained. The *Z*/*E* ratio seems to increase with the solvent polarity, but the reason is uncertain.

Kinetic studies for the amide bond rotation were made for compound **2** in $CDCl_3$. Complete lineshape analysis of the acetyl methyl, *N*-methyl, and 10-H signals at six temperatures between 62 and 23 °C together with the saturation transfer experiments at three temperatures between 23 and 2 °C gave rate constants,[9] which afforded the kinetic parameters for the *E*→*Z* process: $\Delta H^‡ = 69.9 \pm 2.0$ kJ mol^{-1}, $\Delta S^‡ = 11.5 \pm 6.0$ J mol^{-1} K^{-1}, $\Delta G^‡$ (300K) = 66.0 kJ mol^{-1}. The last value is significantly smaller than $\Delta G^‡$ (300K) of 75.1 kJ mol^{-1} for *N*,*N*-dimethylacetamide in dichloromethane,[10] presumably because of the larger ground-state destabilization in **2** due to the bulky Tp group.

Slowing down of the Tp-N bond rotation is observed at low temperatures. In compound **1** existing solely as the *Z*-isomer as well as in the *Z*-isomer of **2**, one of the *o*-benzeno groups is magnetically nonequivalent from the other two at −100 °C in CD_2Cl_2.[11] This is best interpreted as follows. Molecules of **1** are frozen into a geometry similar as in the crystalline state. In *Z*-**2**, the acetyl group is frozen into a notch between two *o*-benzeno groups, while the *N*-methyl group is still rapidly flipping between two sites at −100 °C as shown by **3**.[12] The energy barrier to rotation of the NAc moiety around the Tp-N bond is roughly estimated to be ca. 40 kJ mol^{-1} in either case.



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Further studies including several other *N*-substituted derivatives are in progress.

References and Notes

1 W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970); M. Ōki, “Applications of Dynamic NMR Spectroscopy to Organic Chemistry,” VCH, New York (1985), Chap. 2; M. Pinto, in “Acyclic Organonitrogen Stereodynamics,” ed by J. B. Lambert and Y. Takeuchi, VCH, New York (1992), Chap. 5.

2 See for example: K. B. Wiberg and C. M. Breneman, *J. Am. Chem. Soc.*, **114**, 831 (1992); A. Greenberg, D. T. Moore, and T. D. DuBois, *J. Am. Chem. Soc.*, **118**, 8658 (1996).

3 a) G. Yamamoto, H. Higuchi, M. Yonebayashi, and J. Ojima, *Chem. Lett.*, **1994**, 1911. b) G. Yamamoto, H. Higuchi, M. Yonebayashi, Y. Nabeta, and J. Ojima, *Tetrahedron*, **52**, 12409 (1996).

4 G. Yamamoto, K. Kuwahara, and K. Inoue, *Chem. Lett.*, **1995**, 351; G. Yamamoto, H. Higuchi, M. Yonebayashi, Y. Nabeta, and J. Ojima, *Chem. Lett.*, **1995**, 853.

5 Compound **1**: mp 323−325 °C. Found: C, 84.88; H, 5.66; N, 4.54%. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50%. IR (KBr) 3330, 1658 cm^{-1}. ^1H NMR ($CDCl_3$, 23 °C, 300 MHz) δ 2.52 (3H, s), 5.40 (1H, s), 6.98 (1H, br s), 6.98−7.06 (6H, m), 7.24 (3H, m), 7.40 (3H, m). ^{13}C NMR ($CDCl_3$, 23 °C, 75.5 MHz) δ 169.7 (C=O). Compound **2**: mp 190−191 °C (sublimed sample). Found: C, 84.85; H, 5.96; N, 4.13%. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30%. IR (KBr) 1668, 1650 cm^{-1}. ^1H NMR ($CDCl_3$, 23 °C, 300 MHz) *Z*-isomer: δ 2.59 (3H, s), 3.70 (3H, s), 5.30 (1H, s); *E*-isomer: δ 1.72 (3H, s), 3.85 (3H, s), 5.34 (1H, s). *Z*/*E* = 4.0. ^{13}C NMR ($CDCl_3$, 23 °C, 75.5 MHz) δ 174.5 (*Z*) and 178.0 (*E*).

6 X-ray crystallographic data for compound **1**: $C_{22}H_{17}NO$, FW = 311.39, monoclinic, $P2_1/n$, a = 8.334(6), b = 23.987(11), c = 9.178(5) Å, β = 113.86(5)°, V = 1678(2) Å^3, Z = 4, D_{calc} = 1.233 g cm^{-3}, R = 0.055, 3101 unique reflections with $I > 2.0\sigma(I)$. Data for compound **2**: $(C_{23}H_{19}NO)_2 \cdot H_2O$ (recrystallized from 99% ethanol), FW = 668.84, monoclinic, $P2_1/n$, a = 9.707(1), b = 27.159(8), c = 13.552(2) Å, β = 99.92(1)°, V = 3519(1) Å^3, Z = 4, D_{calc} = 1.262 g cm^{-3}, R = 0.056, 4787 unique reflections with $I > 2.0\sigma(I)$. For both compounds, the structures were solved by direct method (SHELX-86) and all hydrogen atoms were located by difference Fourier synthesis. Full-matrix least-squares refinement was performed with anisotropic non-hydrogen atoms and isotropic hydrogen atoms.

7 Pyramidal nitrogens in lactams are often documented. See for example: T. G. Lease and K. J. Shea, *J. Am. Chem. Soc.*, **115**, 2248 (1993).

8 Theoretical calculations well reproduce the pyramidal nitrogen atom indicating that the pyramidality is the intrinsic property of the molecule and not due to intermolecular interactions.

9 Rate constant/s^{-1} for the *E*→*Z* process (Temp/°C): 300 (62), 170 (52), 80 (44), 40 (38), 18 (28), 12 (23), 4.1 (12.5), and 1.1 (2).

10 K. B. Wiberg, P. R. Rablen, D. J. Rush, and T. A. Keith, *J. Am. Chem. Soc.*, **117**, 4261 (1995).

11 Dynamic behavior of the *E*-isomer of **2** is not clearly observed because of the low population under the conditions.

12 It is assumed that the nitrogen atom in Z-**2** is pyramidal also in solution, though no experimental verification for it is available at present.