Stereochemistry of *N*-Ethyl-*N*-9-triptycylhydroxylamine and Its *O*-Alkyl Derivatives

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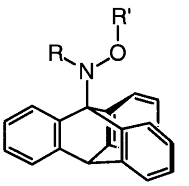
Static and dynamic stereochemistry of the title compounds was studied by X-ray crystallography and variable-temperature NMR. Stereomutation in solution was quantitatively analyzed in terms of two rate processes in which the nitrogen substituents pass over one of the benzene rings of the triptycene skeleton.

In the course of our continuous studies on dynamic stereochemistry of 9-triptycylamine derivatives,[1] we have been interested in derivatives **2**–**4** of *N*-9-triptycylhydroxylamine (**1**: TpNHOH) containing simple alkyl groups.[2] We report here the X-ray molecular structure of the *N,O*-diethyl derivative **4** and dynamic stereochemistry of **2**–**4** in solution.



	R	R'
1:	H	H
2:	C_2H_5	H
3:	C_2H_5	CH_3
4:	C_2H_5	C_2H_5

Compound **1**[3] was treated with ethyl trifluoromethanesulfonate EtOTf to give **2**.[4] Compound **2** was then *O*-alkylated by deprotonation with BuLi or KO^{t}Bu followed by reaction with ROTf (R=Me and Et), affording compounds **3** and **4**.

Figure 1 shows the molecular structure of **4**.[5] The nitrogen atom assumes an almost tetrahedral geometry and the Tp-N bond is completely staggered. The C1–N–O–C7 and C5–N–O–C7 dihedral angles are 148.9° and –89.3°, respectively, which are deviated by ca. 30° from those for the theoretically predicted lowest-energy conformation of hydroxylamine (120° and –120°, respectively).[2] The deviations may be caused by the steric repulsion between the *O*-ethyl group and the Tp skeleton.

^{1}H NMR spectra of **2**–**4** in CD_2Cl_2 at 23 °C indicate the occurrence of fast stereomutation on the NMR time scale: the methylene protons of an ethyl group are mutually equivalent and the three benzene rings of the Tp moiety are also equivalent. Upon lowering the temperature, the lineshape of both the methylene and the aromatic signals broaden, split, and resharpen reflecting the slow-down of stereomutation. At ca. −70 °C each ethyl group affords an ABX_3-pattern signal and three benzene rings of the Tp skeleton are mutually nonequivalent.

Any molecule of **2**–**4** is assumed to exist in one of the conformations schematically shown in Figure 2, which might be similar to the one found in crystal for **4**. Three equivalent conformations and their enantiomeric forms in Figure 2 interconvert by two kinds of rate processes: "R-passing" and "O-passing", where the R group and the OR′ group pass over a Tp benzene ring, respectively. Either process involves inversion of the nitrogen and partial torsion about the N–O bond, which take place either simultaneously or consecutively. The methylene protons of the *N*- and *O*-ethyl groups become equivalent when either of the two processes becomes fast on the NMR time scale, and thus the rate constants obtained by the lineshape analysis (LSA) of the methylene signals correspond to the sum of the rate constants for the two processes. Meanwhile the two processes independently affect the lineshape of the aromatic proton signals and thus the two rate constants can be separately determined from LSA of the aromatic signals.

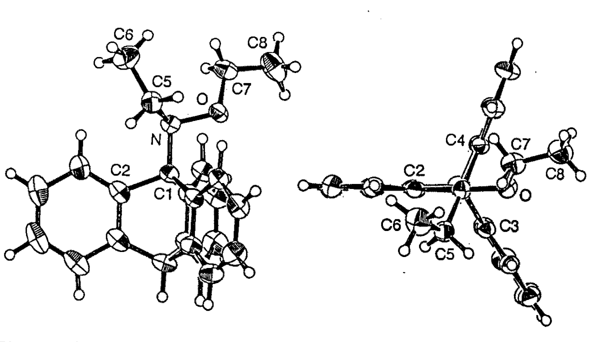
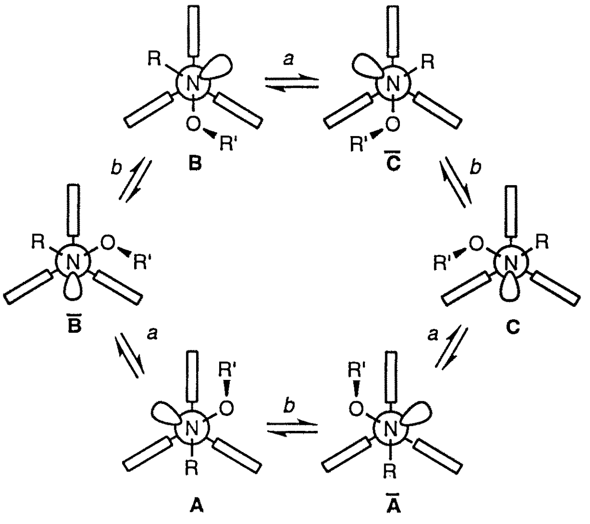


Figure 1. Side and top views of the molecular structure of **4**. Selected bond lengths (Å) and angles (°): N-O, 1.460(2); N-C1, 1.474(2); N-C5, 1.495(2); O-C7, 1.428(2); C1-C2, 1.550(2); C1-C3, 1.548(2); C1-C4, 1.546(2); O-N-C1, 104.4(1); O-N-C5, 107.4(1); C1-N-C5, 114.4(1), N-O-C7, 110.7(1); N-C1-C2, 111.7(1); N-C1-C3, 117.2(1); N-C1-C4, 112.6(1); N-C5-C6, 112.4(1); C1-N-O-C7, 148.9(1); C5-N-O-C7, −89.3(2); O-N-C1-C2, −177.5(1); O-N-C1-C3, 59.5(1); O-N-C1-C4, −63.8(1); C5-N-C1-C2, 65.4(2); C5-N-C1-C3, −57.5(2); C5-N-C1-C4, 179.2(1); N-O-C7-C8, −164.0(2); C1-N-C5-C6, −144.2(2); O-N-C5-C6, 100.5(1).

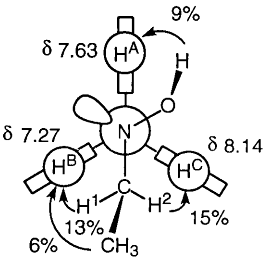


a: "R-passing"; *b*: "O-passing"

Figure 2. Conformations and interconversion processes.

Nuclear Overhauser effect (NOE) experiments at temperatures where the stereomutation is sufficiently frozen revealed the degree of the proximity between the methyl/methylene protons and the *peri*-protons of the Tp skeleton, which enabled the assignments of the *peri*-protons. The results for compound **2** at –72 °C are shown in Scheme 1 as a typical example.[6]

Scheme 1.



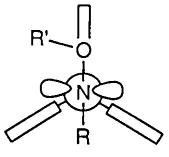
Since the chemical shifts of the three *peri*-protons are firmly assigned for all compounds examined, LSA of the *peri*-proton signals at several temperatures around 250 K affords the rate constants for the two processes, O-passing and R-passing, separately. The rate constants and the free energies of activation at 250 K for both processes in **2**–**4** are shown in Table 1, together with those obtained by LSA of the methylene signals.

Table 1. Rate constants k (s^{-1}) and free energies of activation $\Delta G^\ddagger$ (kJ mol^{-1}) for the two processes at 250 K in CD_2Cl_2 [a]

Compd	O-passing		R-passing		methylene	
	k	$\Delta G^\ddagger$	k	$\Delta G^\ddagger$	k	$\Delta G^\ddagger$
2	13	55.5	81	51.7	93	51.4
3	970	46.6	26	54.1	1000	46.5
4	980	46.5	22	54.5	1000	46.5

[a] The values are calculated by extrapolation of the rate constants obtained by lineshape analysis at several temperatures.

Table 1 shows that the *O*-alkyl compounds **3** and **4** show almost the same kinetic parameters, and that the O-passing is far faster in **3** and **4** than in **2**, while the R-passing is faster in **2** than in **3** and **4**. If we tentatively assume that the transition states for the O-passing and R-passing are schematically shown by **5** and **6**, respectively,[7] the following inferences are made. In the O-passing, the steric congestion around the OR′ moiety will be significantly relieved upon going from the ground state (e.g., **A** in Figure 2) to the transition state **5** and the degree of the relief will be larger in **3** and **4** than in **2**, and thus **3** and **4** will have lower barriers than **2**. In contrast, steric congestion around the OR′ moiety will increase upon going from the ground state to the transition state **6**[7] in the R-passing, and thus the R-passing barrier will be higher in **3** and **4** than in **2**, which is actually observed. Further studies are in progress to verify these speculations.



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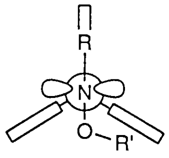

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References and Notes

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4 All new compounds gave satisfactory elemental analyses and spectral data. Compound **2**: mp 219–220 °C. ^1H NMR ($CDCl_3$, 23 °C, 300 MHz) δ 1.62 (3H, t, J = 7.2 Hz), 4.02 (2H, q, J = 7.2 Hz), 5.27 (1H, s), 5.84 (1H, br s), 6.96–7.04 (6H, m), 7.36 (3H, m), 7.69 (3H, br). Compound **3**: mp 275–277 °C. ^1H NMR ($CDCl_3$, 23 °C, 300 MHz) δ 1.80 (3H, t, J = 7.2 Hz), 4.08 (2H, q, J = 7.2 Hz), 4.20 (3H, s), 5.24 (1H, s), 6.94–7.04 (6H, m), 7.34 (3H, m), 7.67 (3H, br). Compound **4**: mp 202–204 °C. ^1H NMR ($CDCl_3$, 23 °C, 300 MHz) δ 1.29 (3H, t, J = 7.2 Hz), 1.78 (3H, t, J = 7.2 Hz), 4.06 (2H, q, J = 7.2 Hz), 4.49 (2H, q, J = 7.2 Hz), 5.24 (1H, s), 6.94–7.03 (6H, m), 7.33 (3H, m), 7.67 (3H, br).

5 X-Ray crystallographic data for compound **4**: $(C_{24}H_{23}NO)_2$, FW = 682.87, triclinic, $P\bar{1}$, a = 13.583(3), b = 15.575(5), c = 8.954(3) Å, α = 91.45(3), β = 90.20(2), γ = 101.71(2)°, V = 1854.2(9) $Å^3$, Z = 2, D_{calc} = 1.223 g cm^{-3}, R = 0.050, wR = 0.127 (on F^2), 6296 unique reflections with $I > 2.0\sigma(I)$. The crystal contains two independent molecules of **4** and their geometries are quite similar to each other. One of them is shown in Figure 1.

6 Separate irradiations of the methylene protons at δ 3.81 and 4.13 enhance two *peri*-proton signals at δ 7.27 and 8.14, respectively, which are reasonably assigned to H^B and H^C, while irradiation of OH enhances the third *peri*-proton signal at δ 7.63 which is uniquely assigned to H^A. The assignments of H^B and H^C come from the following reasonings: Firstly, molecular model considerations indicate that steric repulsion between the methyl and OH groups would tilt the methyl group toward H^B and thus the signal at δ 7.27, which shows NOE upon the methyl-irradiation, should be assigned to H^B. Secondly, the pathways shown in Figure 2 do not exchange H^A and H^B in one step. The reverse assignment, H^B at δ 8.14, contradicts the observed lineshape change.

7 In both transition states **5** and **6**, it is assumed that the nitrogen is planar and the O–R′ bond is periplanar to the lone-pair orbital on the nitrogen in order to minimize the lone-pair/lone-pair repulsion.[2] These structures need further verification.