

¹H-NMR LINESHAPE KINETICS OF INTRAMOLECULAR MOTIONS
BY MEANS OF AN OPTICALLY ACTIVE LANTHANIDE COMPLEX¹⁾

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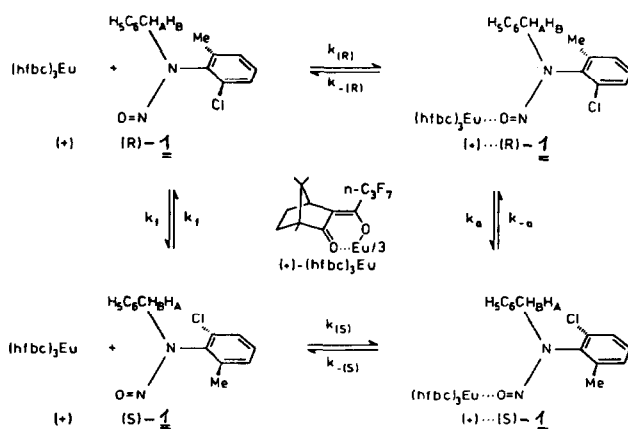
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Optically active auxiliary compounds are useful for the measurement of rates of certain intramolecular motions in chiral and in prochiral molecules⁴⁾, since such additives may generate unequal shifts⁵⁾ for enantiomers or for enantiotopic groups, respectively. This investigation aims to decide whether or not these auxiliary compounds⁶⁾ affect the experimental rate of partial rotation about the aniline single bond in nitrosamines, the N-aryl ring of which is twisted⁹⁾ out of the O-N-N plane.

The free enantiomers (R)-1 and (S)-1⁹⁾ (figure) must have identical δ -values which become unequal by association¹⁰⁾ to (+)-tris[(heptafluorobutyryl)-D-camphorato]europium(III), (+)-Eu(hfbc)₃. The study of temperature-dependent lineshapes of suitable ¹H-nmr signals yield the rate constants k of enantiomerization, i.e. partial rotation. This motion, however, can occur in free 1 (k_f in the figure) and/or in the associated nitrosamine (k_a and k_{-a}). The problem is: Do we measure one process (and which of the two?) or is the experimental k-value a weighted average between k_f, k_a, and k_{-a}? To answer these questions we determined the activation parameters

- without an auxiliary compound,
- in the presence of the racemic compound^{3,12)} (+)-Eu(hfbc)₃, and
- in the presence of the optically active compound¹²⁾ (+)-Eu(hfbc)₃.

1 offers two ¹H-nmr absorptions which are suitable for lineshape kinetics: One AB system for CH_AH_B in the absence of an optically active auxiliary compound and one methyl signal, split into two singlets by the presence of (+)-Eu(hfbc)₃. When the enantiomerization becomes faster, these singlets broaden, coalesce, and form one peak with narrowing linewidth. The same is true for the above AB system in the absence of an additive or in the presence of (+)-Eu(hfbc)₃ (table 1). The shift differences¹³⁾ $\Delta\delta$ and the linewidths b_e in the absence of kinetic broadening were extrapolated to the temperatures where the lines were broadened. For such temperatures, k-values were obtained by complete lineshape analysis¹⁴⁾. The less favorable ratio b_e/ $\Delta\delta$ of the methyl singlets and the smaller temperature range of k-values produce relatively large errors for the ΔH^\ddagger - and ΔS^\ddagger -values of the third column (table 1). The first and second columns show ΔS^\ddagger to be slightly



negative. This is in agreement with values (e.g. ref. 16), obtained for other rotations about sp^2-sp^2 single bonds, starting from non-planar ground states.

The activation parameters (table 1) measured in the presence of $(\pm)-$ and $(+)-\text{Eu}(\text{hfbc})_3$ are identical; they represent a test concerning the unequal molecular probes used (H_A/H_B and $\text{Me}(R)/\text{Me}(S)$, respectively). The agreement with the parameters obtained without an additive is satisfactory. This means¹⁸⁾, contrary to an earlier suggestion¹⁷⁾, that partial rotation in the free nitrosamine (k_f) is rate-determining in the presence of limited amounts of $\text{Eu}(\text{hfbc})_3$. The additional presence of 1:2 association complexes (not shown in the figure) would contribute to the observed induced shifts¹³⁾, but would not alter the above conclusion or the values of table 1. Consequently, the use of $(+)-\text{Eu}(\text{hfbc})_3$ represents a sound kinetic method for the free substrate,

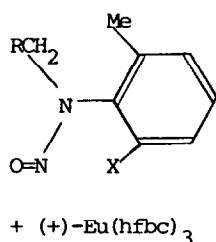
	Auxiliary compound		
	None	$(\pm)-\text{Eu}(\text{hfbc})_3$ (a)	$(+)-\text{Eu}(\text{hfbc})_3$ (a)
Signals used	H_A and H_B (b)	H_A and H_B (b)	$\text{Me}(R)$ and $\text{Me}(S)$
Shift difference $\Delta\delta$	1.634 (17°)	2.681 (22°)	0.120 (10°)
Linewidth b_e	2.4 Hz (17°)	4.2 Hz (22°)	2.4 Hz (10°)
Temperature range of k-values	30° to 130°	27° to 140°	20° to 60° (c)
ΔG^\ddagger (27°) [kcal/mol]	16.46 ± 0.17	16.43 ± 0.17	16.4 ± 0.2
ΔH^\ddagger (27°) [kcal/mol]	14.2 ± 0.8	13.4 ± 1.1	13.3 ± 2.5
ΔS^\ddagger (27°) [e.u.]	-7.4 ± 2.2	-10.4 ± 3.1	-9.5 ± 8.3

Table 1. Lineshape measurements (100 MHz) of partial rotation about the aniline bond in $(RS)-\underline{1}$ (figure). Systematic errors given. Stock solution for all samples: 4.4 mol-% nitrosamines (sum of $\underline{1}$ and its $\underline{2}$ -isomer¹¹⁾), 51.6 mol-% C_4Cl_6 , 40.0 mol-% C_2Cl_4 , and 4.0 mol-% $[\text{CH}_2\text{Si}(\text{CD}_3)_2]_3$. (a): Molar ratio $\text{Eu}(\text{hfbc})_3/\text{nitrosamines}$: 0.24. (b): ${}^2J_{AB} = 14.0$ Hz. (c): $T_c = 37^\circ$.

at least if the latter is similar to 1. In analogy to (RS)-1, the results for 2, (RS)-3, and 4 (table 2) are barriers for the free molecules which, by principle, cannot be studied in the absence of an optically active auxiliary compound. Therefore, this procedure is essential for molecules which do not possess a probe for lineshape analysis, like 2, (RS)-3, and 4, but do so in the presence of a suitable additive.

For non-planar (RS)-1 and (RS)-3 two different planar transition states to rotation are possible, i.e. two pathways may contribute to the experimental barrier, thus rendering strict comparisons of ΔG^\ddagger -values difficult. This statement, however, does not restrict the above conclusions. 2 and 4 can attain only one transition state, thus representing rare cases among non-planar molecules with known barriers to rotation about sp^2-sp^2 single bonds. Accordingly, such molecules of higher symmetry yield unequivocal barriers which, however, are accessible only via association.

Another common auxiliary compound, (+)- $H_5C_6CH(CF_3)OH$, is generally applied in excess^{4,5} in order to generate sufficient shift differences. We suggest rotation in the association complex of this alcohol with 1 to be rate-determining because the barrier is increased¹⁹. Further experiments in this connection are in progress.



	R	X	Solvent	ΔG^\ddagger (36°) [kcal/mol]
(RS)- <u>1</u>	H ₅ C ₆	Cl	CCl ₄ /CFCl ₃ ⁴⁾ or C ₄ Cl ₆ /C ₂ Cl ₄	16.5 ± 0.2
<u>2</u>	H ₅ C ₆	Me	CCl ₄ ⁴⁾	16.7 ± 0.2
(RS)- <u>3</u> ²⁰⁾	H	Cl	C ₄ Cl ₆	15.6 ± 0.3
<u>4</u> ²⁰⁾	H	Me	CCl ₄ ⁴⁾ or C ₄ Cl ₆	16.5 ± 0.2

Table 2. Coalescence measurements¹⁴⁾ of partial rotation about aniline bonds. ΔG^\ddagger -values at T_c were converted to 36° by means of the result (table 1) $\Delta S^\ddagger = -9.5$ e.u. Molar ratio Eu(hfbc)₃/nitrosamines (sum of above compound and its 2-isomer¹¹⁾): 0.24 - 0.30. Signals used: C-Me for 1, 2, and 4; N-CH₃ for 3.

- 1) Application of NMR Spectroscopy of Chiral Association Complexes, Part 4. ----- Part 3: 3.) -----
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- 6) The achiral complex $\text{Eu}(\text{fod})_3$ has been used for determinations of barriers to rotation in amides. Limited amounts of $\text{Eu}(\text{fod})_3$ did not affect the barriers of two amides^{7,8)}.
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- 10) The shifts induced in our nitrosamines and in their Z-isomers¹¹⁾ show that association occurs at the O atom.
- 11) 1 coexists with its Z-isomer (relative to the N-N partial double bond). The barrier⁹⁾ for their interconversion is much higher than the results of tables 1 and 2. The same is true for 2, 3, and 4. The linewidths of the Z-isomers were useful for the extrapolations of b_e to other temperatures.
- 12) We confirm the statement³⁾ of an ^1H -nmr peak originating from our samples of $\text{Eu}(\text{hfbc})_3$ and suspected³⁾ to be due to water. We have now shown by thermogravimetry, ir, and elemental analysis that these samples do not contain a significant amount of H_2O .
- 13) The temperature dependence of induced shifts, irrespective of its causes, is taken into account by the extrapolation of $\Delta\delta$. In ref. 8, the same procedure has been applied to a similar case.
- 14) The "coalescence" of two signals^{15,16,17)} which are generated by an optically active additive must not necessarily be caused by an intramolecular motion. The temperature dependence of their shift difference without additional broadening and narrowing represents an alternative cause. The distinct broadening and narrowing of coalescing signals exclude this alternative for our nitrosamines. In addition, we simulated test lineshapes (cf. ref. 4), as shown by the following example: $\Delta\delta = 0.073$ for the methyl signals of (RS)-1 in the presence of (+)- $\text{Eu}(\text{hfbc})_3$ was obtained by extrapolation to $T_c = 37^\circ$. The broad lineshape at T_c was successfully calculated using $\Delta\delta = 0.073$ and $k = 13.2 \text{ sec}^{-1}$, whereas an elimination of the rotation effect, i.e. $k = 0.001 \text{ sec}^{-1}$, yielded two well resolved signals. Such tests proved that the dependence of $\Delta\delta$ upon T does not contribute to our coalescence phenomena.
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- 18) This conclusion is valid only, if k_a and k_{-a} are smaller than k_f , which seems reasonable when comparing the conjugative possibilities in the transition states of rotation. This consideration is supported by an increase¹⁹⁾ of the barrier in a hydrogen-bonded O-complex of 1 with (+)- $\text{H}_5\text{C}_6\text{CH}(\text{CF}_3)\text{OH}$.
- 19)

	Auxiliary compound	Molar ratio	Solvent	$\Delta G^\ddagger (26^\circ) [\text{kcal/mol}]$
<u>1</u>	(+)- $\text{Eu}(\text{hfbc})_3$	0.28	$\text{CCl}_4/\text{CFCl}_3$	$16.4 \pm 0.2^4)$
<u>1</u>	(+)- $\text{H}_5\text{C}_6\text{CH}(\text{CF}_3)\text{OH}$	5.95	CCl_4	$17.1 \pm 0.3^4)$
- 20) 3, containing 23 % Z-isomer (CCl_4 , 38°): M.p. $34 - 51^\circ$. 4, containing 21 % Z-isomer (CDCl_3 , 26°): Oil. Elemental analyses were correct.