^{13}C DYNAMIC NMR STUDIES ON RESTRICTED ROTATION ABOUT C-N BOND IN CARBAMATES OF THE 9-AZABICYCLO[3.3.1]NONANE SYSTEM[1]

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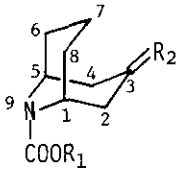
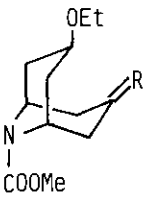
Abstract - ^{13}C NMR spectra of carbamates of the 9-azabicyclo-[3.3.1]nonane and 8-azabicyclo[3.2.1]octane systems have been measured at various temperatures, and their free energies of activation ($\Delta G^{\ddagger}_{C}$) were estimated at the coalescence temperature (T_C) to be 60.6-69.7 ± 0.8 kJ/mol (14.5-16.6 ± 0.2 kcal/mol).

The rotation about C-N bond of amides was studied in detail by means of high resolution NMR spectroscopy with respect to both the amide structure and solvent type.[2] A certain trend between the barrier and the size of N-substituents is suggested; smaller barriers with increase in size of the alkyl group[2,3] and the decreased barrier in amides of cyclic amines due to an $A_{1,3}$ strain[4] operating in the enolate form of the amides considered. The calculation of the free energy of activation ($\Delta G^{\ddagger}_{C}$) for the acetamide of 9-azabicyclo[3.3.1]nonan-3-one from its coalescence temperature (T_C: 86°C) has been reported to be difficult because of the conformational mobility.[5] As the bicyclo[3.3.1]nonane system exists in double-chair conformation at around room temperature,[6] lower T_C (ca. 10-50°C) for the carbamates as compared to those for the corresponding amides makes it easier to estimate the $\Delta G^{\ddagger}_{C}$ values from their T_C.

In this paper we wish to report the rotational barriers in the alkyl 9-azabicyclo-[3.3.1]nonan-3-one-9-carboxylates (1, 2, 3) and in their oximes (4, 5, 6), examined in order to elucidate the effect of the structural constraint on the barrier in the urethane system. Comparison of the $\Delta G^{\ddagger}_{C}$ with those for smaller analogs, ethyl 8-azabicyclo[3.2.1]octan-3-one-8-carboxylate (7) and its oxime (8), or with that for methyl N,N-diisopropylcarbamate (9), an example of acyclic analogs, is also described.



1: R_1=Me, R_2=O
2: R_1=Et, R_2=O
4: R_1=Me, R_2=NOH
5: R_1=Et, R_2=NOH



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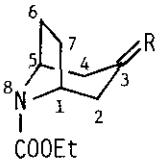
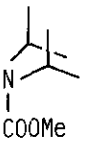
6: R=NOH



7: R=O
8: R=NOH



9

9-Azabicyclo[3.3.1]nonane System

The ^{1}H NMR spectrum of 1 at 0°C exhibits two peaks at 4.68 and 4.79 ppm each representing one proton, assignable to the bridgehead protons at C-1 and C-5. When the spectrum was measured at higher temperatures, both peaks gradually broadened and coalesced into the one at 4.72 ppm at 35°C. From this T_c, the barrier to rotation was calculated to be 65.6 kJ/mol[7] using the expression $\Delta G^{\ddagger}_c = 2.3RT_c(10.32 + \log(T_c/k_c))$, where k_c is the exchange rate given by $k_c = \pi\Delta\nu_{max}/\sqrt{2}$ ($\Delta\nu_{max}$=22.0 Hz for the bridgehead protons of 1). The axial protons at C-2 and C-4, which were also under the influence of rotation of the N-substituent, showed a pair of double doublets at lowered temperatures. Unchanged coupling pattern of some signals over the temperature range 0-40°C, a doublet at δ 2.38 due to the C-2 and C-4 equatrial protons and a multiplet at δ 1.50-1.90 due to the methylene protons at C-6, C-7, and C-8, suggests that the conformation of 1 is of double-chair, which is reported to be most stable among the three possible conformations.[6]

The ^{13}C NMR spectrum of 1 at room temperature showed three broad peaks corresponding to the positions α and β to the nitrogen, each of which was split into two with equal intensity at lowered temperatures. The $\Delta G^{\ddagger}_c$ values (Table: 66.1-66.7 kJ/mol for 1) obtained by the ^{13}C dynamic NMR were in good accordance with that obtained by the ^{1}H dynamic NMR experiments.

Similar behavior was observed in its analogs (2 and 3). Introduction of the exo-substituent at C-7 position, as in compound 3, gave no significant effect on the barrier to restricted rotation. When the carbonyl oxygen at C-3 was substituted by the hydroxyimino group, coalescence was observed with six lines owing to its asymmetric structure, and the T_c for each oxime (4, 5, 6) was higher by ca. 20°C than that for the parent ketone (1, 2, 3). It is interesting to note that the $\Delta\nu_{max}$ values for the syn-carbons (C-2) were smaller by 5-6 Hz than those for anti-ones (C-4) in every case, which would be another method[8] for discrimination of these carbons.

Table Spectral Data and Free Energies of Activation ($\Delta G^{\ddagger}_{c}$) Estimated at the Coalescence Temperature (T_c).

Compd.	Position	$\Delta\nu_{max}$ (Hz)	T_c (K)	$\Delta G^{\ddagger}_{c}$ (kJ/mol)
	1,5	22.0	313	66.7
1	2,4	10.3	302	66.1
	6,8	13.2	306	66.4
	1,5	23.4	310	65.8
2	2,4	8.8	298	65.6
	6,8	13.2	301	65.3
	1,5	8.8	297	65.4
3	2,4	11.7	300	65.2
	6,8	13.2	302	65.5
	1	25.6	328	69.6
	2	13.2	318	69.1
4	4	18.3	323	69.4
	5	27.1	327	69.2
	6	14.6	320	69.3
	8	15.4	320	69.2
	1	27.8	329	69.6
	2	12.5	317	69.0
5	4	18.3	324	69.6
	5	28.6	330	69.7
	6	13.9	319	69.2
	8	14.7	319	69.1
	1	15.4	317	68.5
	2	13.2	315	68.4
6	4	19.0	320	68.6
	5	16.1	319	68.8
	6	15.4	319	68.9
	8	14.7	318	68.8
	1,5	-	-	
7	2,4	24.9	287	60.6
	6,7	41.0	295	61.2
	1	-	-	
	2	24.2	287	60.7
8	4	29.3	290	60.9
	5	-	-	
	6	36.6	293	61.0
	7	36.6	293	61.0
9	α	52.0	288	59.1
	β	39.6	285	59.1

8-Azabicyclo[3.2.1]octane System

Estimation of the $\Delta G^{\ddagger}_{c}$ values for 7[9] and 8 by either α-carbons (C-1 or C-5) or α-protons was difficult in their ^{13}C and ^{1}H NMR experiments owing to their small $\Delta\nu_{max}$ values[10] and to the large half- and base-widths of the spectral lines.[11] Lower T_c as compared to their analogs (1 - 6) were obtained for the carbons at 2, 4, 6, and 7 in their ^{13}C dynamic NMR experiments. The $\Delta G^{\ddagger}_{c}$ values calculated from T_c were ca. 60.6-61.0 kJ/mol.

Conclusion

The activation energy for the COOMe rotation in 9 was calculated from the T_c for the α and β carbons to be 59.1 kJ/mol.[12]

In consequence, relatively large $\Delta G^{\ddagger}_{c}$ values (65.2-69.7 kJ/mol) among carbamates (58-67 kJ/mol for simple carbamates)[13] were obtained for the bicyclo[3.3.1]nonane system. The distinct enhancement of the $\Delta G^{\ddagger}_{c}$ for the system in comparison with those for bicyclo[3.2.1]octanones may be ascribed to the steric hindrance between the four exo protons at C-2, C-4, C-6, and C-8 positions and the carbomethoxyl in the transition state where the COOR plane is perpendicular to the C-1, N, and C-5 plane. It is noteworthy that, in the bicyclo[3.3.1]nonane system, the barrier to rotation is affected by modification of the functionality at the position γ to the nitrogen. The correlation between the type of the functional moieties at C-3 and the rotational barrier in this system is under investigation.

Experimental conditions are as follows: The ketones used for the experiments were synthesized according to the known methods (1,[14] 2,[15] 3,[16] 7,[17]). The oximes were prepared by treatment of them with hydroxylamine hydrochloride in the presence of sodium acetate. NMR spectra were measured on a JEOL JNM-FX 200, operating at 199.5 MHz for ^{1}H and 50.1 MHz for ^{13}C nuclei. Temperatures were controlled by a JEOL PVT-32 temperature control unit, and the sample temperatures were determined by a thermometer (Shigemi NMR thermometer TM-003) placed within the 10-mm sample tube. The compounds were dissolved (0.3 M) in Chloroform-d_1 and TMS was used as an internal standard.

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