

MAGNETIC NON-EQUIVALENCE OF METHYLENE PROTONS OF *N*-BENZYL GROUP IN *N*-BENZYL AZIRIDINES AND THEIR ADDUCTS

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Abstract : The magnetic non-equivalence of the benzyl methylene protons of *trans*-1-benzyl-2,3-diphenylaziridine and *erythro*-1-benzyl-2-cyano-3-phenylaziridines, as well as the related cycloadducts, has been investigated by means of dynamic ¹H NMR spectroscopy. It is postulated that the diastereotopic origin of the benzyl methylene protons of the foregoing two compounds arises from n-π electronic interactions.

Introduction

The study by Bottini and Roberts of the nitrogen inversion process of 1-alkylaziridines by utilizing variable ¹H NMR¹ initiated extensive interest by other investigators.²⁻⁴ It is well known that inversion about nitrogen is a relatively slow process for some aziridines.⁵ Kinetically formed invertomer ratios were investigated by NMR.⁶ Of note, is the isolation of invertomers of *N*-chlorobenzoylphenylaziridine.⁷

Determination by NMR of the rotational barrier in amides such as *N,N*-dimethylacetamide is well established. Indeed, the study is an example of dynamic NMR spectroscopy at undergraduate level.⁸ Although it is rather well documented that methylene protons (¹H NMR) split to an AB quartet in some compounds possessing an *N*-benzyl group, the reason is not always clear. For example, as a result of the lack of a plane of symmetry in α, α'-*trans*-disubstituted heterocyclic amines, the methylene protons of their *N*-benzyl derivatives are stereochemically and magnetically non-equivalent. These phenomena are considered not to be restricted to an asymmetric carbon. Instead it is determined by dissymmetry of a methylene moiety rather than restricted rotation.⁹ Therefore, the *N*-benzylmethylene ¹H NMR signal has often been believed to serve as establishing the stereochemistry of *N*-benzylpiperidines and *N*-benzylpiperidones.^{9a, b}

However, little is known about magnetic nonequivalence of methylene protons in *N*-benzylic groups. During the course of our studies on synthesis of fused heterocycles employing 1,3-dipolar cycloadditions of cycloimmonium and related azomethine ylides with dibenzoyl acetylene, we have found that some *N*-benzylaziridines and one of their cycloadducts, which are readily available by 1,3-dipolar cycloadditions of the present aziridines with dibenzoyl acetylene, indicated magnetic non-equivalence of methylene protons of an *N*-benzyl moiety. Whereas the ¹H NMR signal appeared as an AB quartet, others did not show such phenomena.^{10,12} These phenomena are the subject of the present paper.

Results and Discussion

cis- and *trans*-1-Benzyl-2,3-diphenylaziridines *cis*-**1** and *trans*-**1** were stereospecifically prepared by an established method.¹³ In the case of *cis*-**1**, both benzylic methylene and ring protons show sharp singlets at δ 3.86 and 3.04, respectively, while those of *trans*-**1** appear at δ 3.63 and 3.33 as an AB quartet (*J*=14.4) and a broad doublet around 3.20 and 3.38. This ¹H NMR behavior of *cis*-**1** is apparently natural because of its symmetry character, i.e. the inversion at the benzyl nitrogen is confined in one direction. In contrast, ¹H NMR of the ring protons of *trans*-**1** shows, at 4 °C, AB-q at 3.42 and 3.18 (*J*=3.3 Hz)

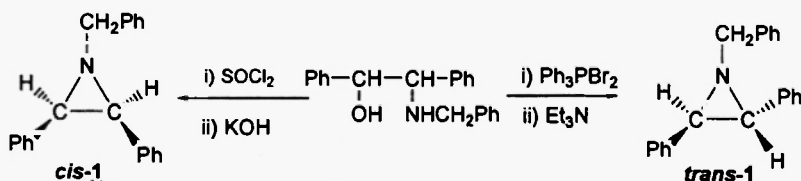
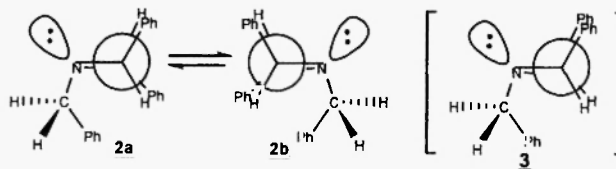


Table-1 : Summary of ^1H NMR data of **1**

	<i>cis</i> - 1	<i>trans</i> - 1
mp. ($^{\circ}\text{C}$)	43-44	68-70
^1H NMR (CDCl ₃) at rt	7.02-7.52(m) 3.86 (s) 3.04 (s)	7.2-7.4(m) 3.63, 3.33 (ABq, J=14.4) (2H, Benzyl H) 3.20, 3.38 (brd) (2H, ring H)

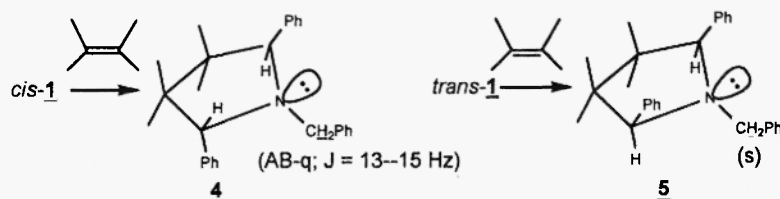
which underwent coalescence at 38 $^{\circ}\text{C}$ to give a singlet. A value of 15.7 kcal/mol was determined for ΔG^{\ddagger} , the energy barrier of inversion at nitrogen. Intriguingly, in nitrobenzene at room temperature a solvent-effect manifested itself as a sharp singlet, a phenomenon that indicates $n-\pi$ interaction, **2**, as shown in Scheme-2. While the invertomers of *trans*-**1** are essentially equivalent, the lack of a plane of symmetry resulted in splitting of the ring protons in the NMR spectrum as an AB quartet. Indeed, this AB quartet did not undergo coalescence in nitrobenzene even at 160 $^{\circ}\text{C}$. It is noted that both of the invertomers **2a** and **2b** suffer steric interaction between the benzyl and one phenyl groups, while *cis*-**1** might take an exclusive conformation **3** because of steric repulsion between the benzyl and two phenyl groups.¹⁴



2 in CDCl₃. Ring protons
 at 38 $^{\circ}\text{C}$ 3.26 (coalescence)
 at 4 $^{\circ}\text{C}$ 3.42, 3.18 (AB-q; J=3.3 Hz)
 $\Delta G = 15.7$ kcal/mol
 $T_c = 38$ $^{\circ}\text{C}$
Methylene protons
 3.66, 3.31 (AB-q; J=14.4 Hz)
 in PhNO₂: at rt (23.5 $^{\circ}\text{C}$)
Ring protons: 3.30 (sharp s)
Methylene protons
 3.62, 3.47 (AB-q; J=14.4 Hz)

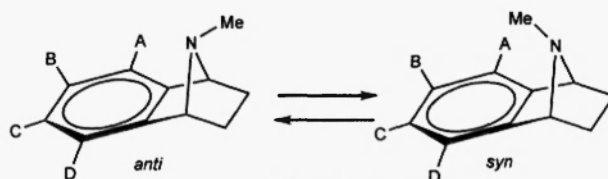
Scheme-2

cis- and *trans*-**1** underwent stereospecific 1,3-dipolar cycloaddition both with respect to **1** and dipolarophiles such as dimethyl fumarate, dimethyl maleate, and fumaronitrile to produce the corresponding pyrrolidines **4** and **5**, respectively.¹³ Regardless of configuration at 3- and 4-positions, the methylene protons show AB-q when phenyl groups at α , α' -positions are *trans*, whereas those of *cis*-isomers appear as a singlet. Thus, it is suggested that non-equivalence of benzyl methylene protons might not originate from a dissymmetric moiety of the molecules but from restricted rotations either impeded by steric factors or $n-\pi$ interaction.



Scheme-3

In the initial study of restricted nitrogen inversion in *N*-methylpolyhalobenz-7-azanorbornadienes (Scheme 4), the *anti* conformer was believed to be the dominant form based upon a presumed attractive lone pair/benzene ring interaction ($n-\pi$ interaction). However, it was demonstrated by the same group that the *syn* conformation is the preferred invertomer.¹⁵ Therefore, $n-\pi$ interaction was not sufficiently strong to determine the conformation, a phenomenon which is also evident in this case.



Scheme-4

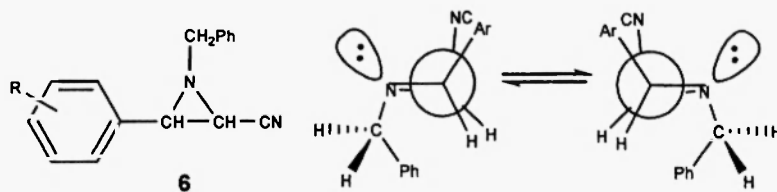
An evaluation of temperature dependent $^1\text{H-NMR}$ analyses of benzyl methylene for *erythro*-1-benzyl-2-cyano-3-phenylaziridines **6**¹² was undertaken. The results are compiled in Table 2.

Table-2 : Temperature dependent $^1\text{H NMR}$ analyses of benzyl methylene protons of **6**

R	Solvent ^a	Temp (°C)	T _c (°C)	δ_{TMS}	J _{AB} (Hz)	ΔG^\ddagger (kcal/mol)
H	C	-24 ~ rt	8	3.75, 3.68	13.5	14.0
<i>o</i> -Cl	C	rt ~ 79	65	3.79, 3.68	13.7	16.9
<i>p</i> -Cl	N	rt ~ 61	36	3.95, 3.87	13.6	15.4
	C	rt ~ 99	---	3.78, 3.69	13.7	>18
<i>p</i> -Me	N	rt ~ 100.5	88	3.97, 3.86	13.2	18.1
	C	5 ~ 32.5	24	3.74, 3.66	13.7	14.8
<i>p</i> -MeO	C	2 ~ rt	20	3.75, 3.67	13.8	14.6

^a C: CDCl₃, N: nitrobenzene

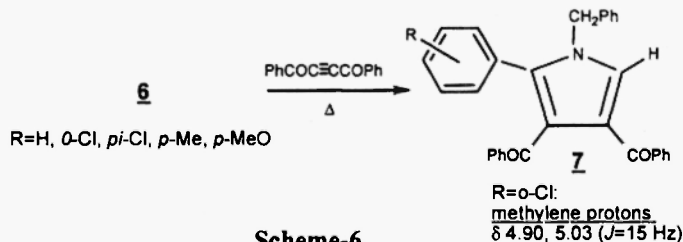
The restricted rotational process of the benzyl methylene protons is complicated because it is coupled to the nitrogen inversion process as shown in Scheme 2 and Scheme 5. Thus, it is not easy to explain a substituent effect on the coalescence temperature (T_c) and the activation energy barrier (ΔG^\ddagger). An electron withdrawing group such as Cl presumably increases n- π interaction so that the benzyl methylene protons become more diastereotopic as the nitrogen inversion process becomes slow.



Scheme-5

It is interesting to note that in the highly congested 9-benzyltricyclicene, the ΔG^\ddagger value for the rotational barriers of the benzyl methylene was estimated to be 16.1 kcal/mol based on dynamic NMR spectral analyses.^{9e} The value is comparable with those we report for *N*-benzyl aziridines.

Finally, among the pyrroles **7** (Scheme 6) obtained by 1,3-dipolar cycloadditions of **6** with dibenzoylacetylene,¹² only the *o*-chlorophenyl pyrrole exhibited ABq in $^1\text{H NMR}$ spectrum of the benzyl methylene protons. This is perhaps simply attributed to steric hindrance of rotation of the methylene protons by an *o*-chloro substituent.



Scheme-6

In any event, the methylene protons that are in a diastereotopic environment would be nonequivalent and therefore an ABq pattern would be expected. The origin for the diastereotopic environment is presumed to arise not only from the presence of dissymmetric moiety but also from the restricted rotation caused by n- π interaction and steric hindrance.¹⁶

Experimental

Compounds **1**, **4**, **6**, and **7** were prepared as previously described.^{12, 13} NMR spectra were recorded on a Jeol JNM-4H-100 operating at 100 MHz and referenced to SiMe₄ (δ in ppm and *J* in hertz).

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