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STRUCTURAL ANALYSIS OF 2-(2,4,5-TRIPHENYL-1H-IMIDAZOL-1-YL)ETHAN-1-OL

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Theoretical NMR shifts and coupling constants of 2-(2,4,5-triphenyl-1H-imidazol-1-yl)ethan-1-ol have been calculated through the use of B3LYP/EPR-III level of theory in DMSO medium. It found that the gauche conformer is 1.5 kcal/mol more stable than anti-conformer. The calculation fairly matches with obtained X-ray structure. Based on Boltzmann relationship, the gauche and anti-structure population was observed conformably to theoretical NMR shifts. Note that the theoretical and experimental NMR shifts and coupling constants were in a good agreement with each other.

Keywords: *gauche conformer, anti-conformer*

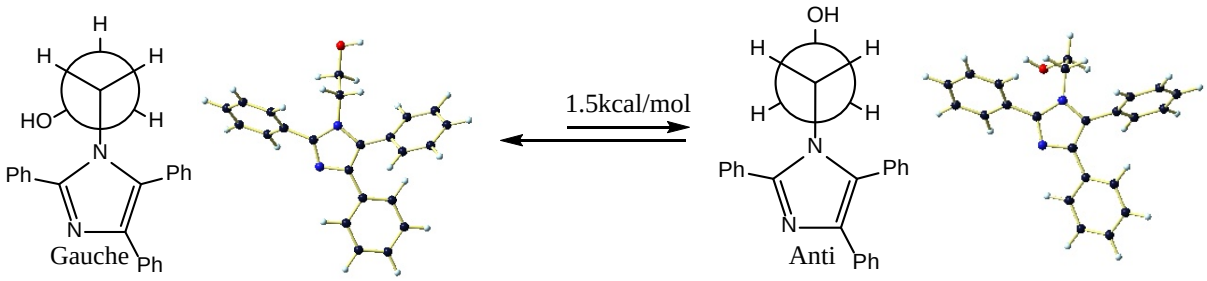
INTRODUCTION

Imidazoles are important compounds for drug design. They are used as antifungal [1], anti-inflammatory [2], antibacterial [3] and anticancer [4] agents. Imidazole scaffold is also required for preparation of ionic liquids which is thought to be a valuable solvent and catalyst in organic synthesis. Considering the importance of the compounds stated above, imidazoles have become a challenge for many scientists in terms of synthesis and structural analysis [5].

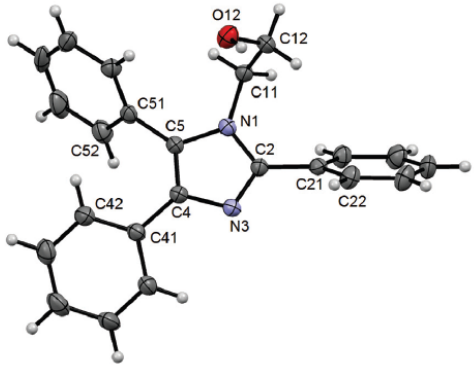
We chose 2-(2,4,5-triphenyl-1H-imidazol-1-yl) ethan-1-ol to inquiry into its theoretical and X-ray structure as well as identify correlation between theoretical and experimental NMR shifts.

RESULTS AND DISCUSSION

We optimized gauche and anti-conformers of 2-(2,4,5-triphenyl-1H-imidazol-1-yl)ethan-1-ol, to reveal that the gauche conformer is 1.5 kcal more stable than the anti-conformer in DMSO medium (Scheme 1). This is expected since the X-ray structure (Scheme 2) is found to be in the gauche conformation in the solid phase. The only difference between these two conformers is hydroxyethanyl (HO-CH2-CH2-N) group orientation in space. Herein, we focus on this moiety in order to reveal relationship between experimental and theoretical results.



Scheme 1. Optimized structures of anti and gauche conformers of 2-(2,4,5-triphenyl-1H-imidazol-1-yl)ethan-1-ol in DMSO (using SMD salvation method) at the B3LYP/6-31G* level of theory.



Scheme 2. X-ray structure of 2-(2,4,5-triphenyl-1H-imidazol-1-yl)ethan-1-ol.

Conformer populations are calculated by the Boltzmann equations (Eq 1 and 2) as follows:

$$\frac{\eta_g}{\eta_a} = e^{-\Delta G/RT} \qquad \text{Eq 1}$$

$$\eta_g + \eta_a = 1 \qquad \text{Eq 2}$$

As a result, we found that the gauche conformer population is 93% in DMSO. We noticed that population percentages are applicable to the gauche and anti-conformers as theoreticalNMR shifts as well as to $^3J_{HH}$ coupling constants of the hydroxyethanyl moiety of the product. The $^3J_{HH}$ theoretical values are obtained for each conformer at the B3LYP/EPR-III level of theory. This is done because of their combination used in the newest literature for NMR prediction of organic molecules [6].

The contribution of each conformer to the observed $^3J_{HH}$ and δ_{CH_2} can be estimated by the following equations (Eq 3 and 4):

$$^3J_{HH} = \eta_g\ ^3J_{HH(gauche)} + \eta_a\ ^3J_{HH(anti} \qquad \text{Eq 3}$$

$$\delta_{CH_2} = \eta_g \delta_{CH_2(gauche)} + \eta_a \delta_{CH_2(anti} \qquad \text{Eq 4}$$

This is effective where η_g and η_a represent the populations, as well as $^3J_{HgHg}$ or $^3J_{HaHa}$ values of the intrinsic ^3J of the conformer *gauche* and *anti*, respectively. As seen from the experimental ^1H NMR shifts (see below), hydrogens of methylene carbons are chemical and magnetic equivalents, since the coupling patterns are triplet for CH_2 bonded to nitrogen and quartet for CH_2 bonded to hydroxyl group. In the table below, intrinsic ^3J values and chemical shifts are listed for each conformer. Their contribution to the total theoretical value based on the population of each conformer is shown in the equilibrium.

Intrinsic ^3J values and δ_{CH_2} for each conformer and its contributionto the theoretical $^3J_{HH}$ value (Hz) and δ_{CH_2} (ppm) weighted by conformer population.

$\delta_{(anti)}$	$\delta_{(gauche)}$	$\delta\eta_a$	$\delta\eta_g$	δ(calc.)	δ(exp.)	hydroxyethanyl
3.70	3.22	0.27	2.99	3.26	3.22	HO-CH_2-CH_2-N

3.50	3.62	0.25	3.36	3.61	3.98	$HO-CH_2-CH_2-N$

$^3J_{HH(gauche)}$	$^3J_{HH(anti)}$	$^3J_{HH(gauche)}$	$^3J_{HH(anti)}$	$^3J_{HH}$(calc.)	$^3J_{HH}$(exp.)
5.4	9.2	5.0	0.6	5.6	6.4

Experimental ^1H ^{13}C NMR shifts and coupling constants of 2-(2,4,5-triphenyl-1H-imidazol-1-yl)ethan-1-ol

^1H NMR (500 MHz, DMSO) δ 7.80 (d, *J* = 7.1 Hz, 2H), 7.58 – 7.44s (m, 8H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 4.87 (t, *J* = 5.4 Hz, 1H), 3.98 (t, *J* = 6.4 Hz, 2H), 3.22 (q, *J* = 6.2 Hz, 2H).

^{13}C NMR (75 MHz, DMSO) δ 147.58, 137.02, 135.20, 131.73, 131.58, 131.47, 130.27, 129.53, 129.30, 129.11, 128.96, 128.49, 126.57, 126.52, 59.78, 46.95.

The intrinsic ^3J value for the anti-conformer is larger than that for the gauche, which corroborates the Karplus relationship for $^3J_{HH}$ [7]. The theoretical $^3J_{HH}$ is close to the value measured in the experimental ($^3J_{HH}$ = 6.4 Hz). (See above for experimental NMR data) to reaffirm the fact that in DMSO solution the hydroxyethanyl radical of the tetra-substituted imidazole is in the gauche conformation.

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2-(2,4,5-TRİFENİL-1H-İMİDAZOL-1-İL)ETAN-1-OLUN STRUKTUR ANALİZİ

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Az1025 Bakı, Xocalı prospekti, 30

2-(2,4,5-trifenil-1H-imidazol-1-il)etan-1-olun nəzəri NMR parametrləri B3LYP/EPR-III metodu ilə DMSO mühitində hesablanmışdır. Qaus konformasiyasının antidən daha stabil olduğu müəyyənləşdirilmişdir. Boltzman əlaqəsi əsasında Qaus və anti konformasiyalarının papuliasiya analizi edilmiş və NMR parametrlərin tətbiq edilmişdir. Nəzəri olaraq əldə edilmiş nəticə praktiki NMR parmetrləri ilə üst-üstə düşmüşdür.

Açar sözlər: *konformasion analiz, Qaus konformasiyası, anti-konformasiya*

СТРУКТУРНЫЙ АНАЛИЗ 2-(2,4,5-ТРИФЕНИЛ -1H-ИМИДАЗОЛ-1-ил) ЭТАН-1-ОЛА

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Вычислены теоретические ЯМР-параметры 2-(2,4,5-трифенил-1н-имидазол-1-ил) этан-1-ола методом B3LYP/EPR-III в среде ДМСО и установлено соответствие экспериментальных и теоретических данных.

Ключевые слова: *конформационный анализ, гауссова конформация, антиконформация.*

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