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The Effect of Long-Range Circumannular Non-Bonding Orbital Interaction on the Inversion of Groups on Nitrogen in 2,2,4,4-Tetramethyl-3-imino-1-cyclobutanones

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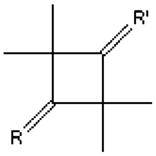
ABSTRACT



I. R=O, R'=Cyclohexyl III.R=O, R'=Phenyl
II. R=CH_2, R'=Cyclohexyl IV. R=CH_2, R'=Phenyl

The free energy of activation, Δ*G, for nitrogen inversion was calculated from the coalescence temperature for the methyl signals obtained via variable temperature NMR for a series of imino derivatives of the title compounds. There was a direct correlation between the long-range nonbonding circumannular orbital interactions between the heteroatoms in the 1,3-positions and the Δ*G** for inversion of groups on nitrogen. Values of Δ*G** range from 26 kcal/mol on systems with maximum interaction in the transition state (I and II) to 17 kcal/mole on those systems with minimal interaction (III and IV).**

Synthesis, spectroscopy, and chemistry of simple imines is well documented,[1] and inversion through nitrogen is a common theme. Similar studies on the title compounds are available and include spectroscopy[2,3] and circumannular and transannular orbital interactions. Photoelectron spectroscopy clearly established that the nonbonding lone pair orbitals interact to give a symmetric and asymmetric pair of distinct nonbonding molecular orbitals.[4] This discovery of two different nonbonding energy levels was a significant finding and explained the observed ultraviolet absorption spectroscopy. There is no previous evidence in the literature on whether the long-range nonbonding orbital interactions affect physical or chemical behavior of the title compounds. In recent work we described the affect of these orbital interactions on the chemistry of the carbonyl chromophore in the monoimines, and depending on the magnitude of the nonbonding interaction, the carbonyl behavior was altered. The greater the interaction, the more the carbonyl group deviates from normal chemical behavior.[5]

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[5] Naik, A.; Ferro, M.; Worman, J. J. 217th National Meeting of the American Chemical Society, San Francisco, March 1999, Abstract 0198. Naik, A., M.S. Thesis, *The Study of Circumannular Orbital Interactions in the Imine Derivatives of 2,2,4,4-Tetramethyl-1,3-cyclobutanedione*, Rochester Institute of Technology, Rochester, NY, 1998.

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The purpose of this study was to show that the nonbonding orbital interactions have an effect on the free energy of activation for the inversion of the group attached to nitrogen on the monoimines.

All compounds were prepared by a standard synthetic technique of refluxing the diketones in toluene with a slight excess of the amine, in the presence of a catalytic amount of *p*-toluene sulfonic acid,; water is azeotroped off using a Dean Stark trap. Evaporation of toluene in vacuo followed by sublimation and recrystalization gives most products in 60% yield. Synthesis, spectral properties, and elemental analysis for compounds I−IV were consistent with the structures and identical to those reported in the literature.[5−7]

At room temperature the methyl groups on the monoimines gave two distinct singlet resonances that gradually coalesce as the temperature is increased. All NMR spectra were observed in d_6-DMSO on a Bruker 300-MHz spectrometer. The temperature was increased from 20 to 190 °C, and the NMR spectra were observed at 10° intervals until coalescence was attained. The original data and spectra can be found elsewhere.[5]

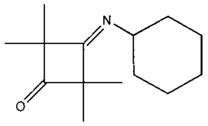
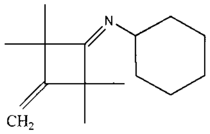
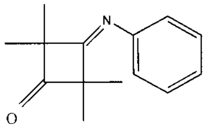
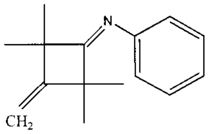
The free energy of activation, ΔG^*, for compounds I−IV was calculated using the following formula:

$$\Delta G^* = 2.3RT_c(10.32 + \log T_c/k)$$

where ΔG^* is the free energy of activation, R is the universal gas constant, T_c is the temperature of coalescence, and k is the rate of inversion at slow exchange.

Values of ΔG^* for the imine derivatives are listed in Table 1.

Table 1. Free Energy of Activation (ΔG^*) Values for the Various Imine Derivatives

		ΔG^* (kcal/mol)
I		26.13
II		22.17
III		17.71
IV		17.36

The fact that phenyl imine derivatives require less activation energy for nitrogen inversion than those containing the cyclohexyl group can be explained by less repulsion in the transition state as a result of resonance stabilization. If the R group on nitrogen inverts mainly via a translational mechanism, the transition state will have the nonbonding orbitals on nitrogen change from sp^2 hybrid orbitals to p orbitals and back to sp^2 (Figure 1).

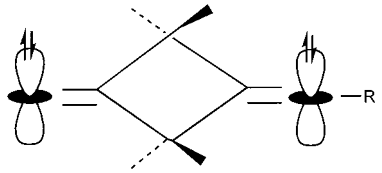


Figure 1.

When the substituent is phenyl the lone pair on nitrogen will be delocalized into the ring, thus decreasing the orbital repulsion with the lone pair on oxygen. The ΔG^* of activation for nitrogen inversion should be less for the phenyl derivatives and greater when R = cyclohexyl where maximum repulsion is predicted, and this is observed.

To further support the hypothesis, the carbonyl was converted to a methylene group; this would preclude lone pair interaction in the transition state and the free energy of activation should decrease, which is consistent with the observed results. Electron-withdrawing and -donating groups on the phenyl rings are presently being examined, and the data supports the hypothesis that long-range nonbonding orbital interactions affect the inversion of groups on nitrogen in the title compounds. The results from this study were presented recently.[8] One might argue that there is also a rotational component to the inversion. We examined the magnitude of this interaction by preparing the *N*-oxide of the cyclohexyl imino cyclobutanone[9,10] and observing the methyl coalescence where the only component to the inversion mechanism would be rotation. The coalescence temperature was not measurable within the limits of the instrument. An extrapolated T_c value allowed us to calculate ΔG^* and conclude that a minimum of 30 kcal/mol would be required for rotation.[9] This is far above that observed for the free imine, and at best would only play a minimum role in the overall inversion mechanism.

Another point of discussion could reflect on the transannular interaction via the p-π orbitals. However, for the most part the interaction of the p-π orbitals with the orthogonal nonbonding orbitals should be non-existent or at least constant since all compounds examined contain 2p−2p type π bonds.

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Long-range nonbonding orbital interactions in 2,2,4,4-tetramethyl-3-iminocylcobutanones affect the free energy of activation for inversion of substituents on the nitrogen atoms. Lone pair–lone pair repulsion in the transition state can account for the observed results.

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Supporting Information Available: Synthesis and characterization data of compounds I–IV and the *N*-oxide of I. This material is available free of charge via the Internet at http://pubs.acs.org.

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