Research Article

Magnetic Resonance in Chemistry

Received: 11 January 2008 Revised: 24 April 2008 Accepted: 25 April 2008 Published online in Wiley Interscience: 3 June 2008

(www.interscience.com) DOI 10.1002/mrc.2259

Conformational and structural analysis of exocyclic olefins and ketimines by multinuclear magnetic resonance

Rubén Montalvo-González,[a] J. Ascención Montalvo-González[b] and Armando Ariza-Castolo[b]*

The ^{1}H, ^{13}C, and ^{15}N NMR spectra of 5 exocyclic alkenes and 15 different ketimines obtained from cyclohexanone and derivatives using benzyl bromide and primary amines – are analyzed. Relative stereochemical and preferential conformations are determined by analyzing both the homonuclear coupling and the chemical shifts of the protons and carbon atoms in the aliphatic rings, which are directly related to the geometry of the double bond and the steric and electronic effects of the exocyclic group. In addition, the racemic mixture of the *N*-(4-methylcyclohexylidene)pyridine-3-amine derivative is resolved.

Supporting information may be found in the online version of this article.

Keywords: NMR; ^{1}H; ^{13}C; ^{15}N; chiral axis; conformation; alkenes; ketimines

Introduction

The NMR is a powerful tool in determining the preferred conformation, the stereochemistry of a compound, and the stereoselectivity of reactions.[1] Several works have been published regarding both nucleophilic attacks on an exocyclic double bond, namely C=N, and the effects that the N-group may have on the regioselectivity (axial/equatorial) of imine compounds similar to those reported herein.[2] However, in order to determine the preferential conformation, a more detailed analysis is required.

Saito and Nukuda determined the geometry of the exocyclic C=N double bond of compound **1a**, and the preferential orientation of the phenyl group with respect to the double bond, by using ^{1}H NMR and UV spectroscopy.[3] In this article, we describe the preferential orientations of aryl groups with respect to an exocyclic C=C or C=N double bond and the orientations and effects of the cyclohexenyl substituents on the chemical shifts and coupling constants of the aliphatic ring.

Unfixed (R_1 = H) and fixed (R_1 = methyl or *tert*-butyl) compounds were used for the structure analyses. These compounds had either an aryl (**1a–e, 2a–e**, and **3a–e**) or an alkyl (**4a–e**) substituent bonded to the exocyclic atom of the C=C (alkenes) or C=N (imines) double bond (Scheme 1). Assignment of the ^{1}H spectra of olefin and imine derivatives obtained from symmetric ketones (**1a, 1d, 1e, 2a, 2d, 2e, 3a, 3d, 3e, 4a, 4d**, and **4e**) was carried out based on simulations. Furthermore, the two enantiomers of **3d** were resolved using the lanthanide shift reagent ytterbium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate].

Results

Assignment of the ^{1}H and ^{13}C spectra of alkenes and imines was based on one- and two-dimensional NMR experiments. The connectivities were established by means of homonuclear $^{1}H-^{1}H$ (COSY) and heteronuclear $^{1}H-^{13}C$ (HETCOR) correlation spectroscopy. The selected pulse sequence was applied because a high resolution in ^{13}C is necessary due to the fact that the chemical shift differences of some resonances are less than 0.02 ppm (<2 Hz at 75.47 MHz). Also, *J*-modulated spectra attached proton test, (APT) were recorded to distinguish between the C, CH, CH_2, and CH_3 groups in compounds **1b–e, 2b–e, 3b–e,** and **4b–e**.

The exocyclic substituent (R_2) effect on the atoms of the cyclohexenyl moiety of alkenes and imines was based on the change in the chemical shift of the *equatorial/axial* protons of C2 and C6 in olefins and imines derived from symmetric ketones (**1a, 1d, 1e, 2a, 2d, 2e, 3a, 3d**, and **3e**).

Chiral conformers (**1a, 2a, 3a**, and **4a**) were derived from cyclohexanone exchange because of the fast ring inversion at 20 °C.[4] In contrast, compounds with a methyl or *tert*-butyl group on the aliphatic ring have a conformational preference for the structure with the alkyl group at the equatorial position. Alkenes and imines derived from symmetric ketones are asymmetric compounds obtained as pairs of enantiomers (*Ra* and *Sa)* in a racemic mixture. This fact was demonstrated by the addition of a chemical shift reagent to the imine compound **3d**, which allowed separation of the enantiomer in the proton spectra.

Derivatives of 3- or 2-methylcyclohexanone have two pairs of geometric isomers (namely, *ER, ES, ZR*, and *ZS*). The ratio between

* *Correspondence to: Armando Ariza-Castolo, Centro de Investigación y de Estudios Avanzados del IPN, Apartado Postal, 14-740, 07000, México D.F., Mexico. E-mail: aariza@cinvestav.mx*

a *Unidad Académica de Ciencias Químico Biológicas y Farmacéuticas Universidad Autónoma de Nayarit, México*

b *Departamento de Química, Cinvestav. Apartado postal, 14-740, 07000 Mexico D.F., Mexico*