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

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The <sup>1</sup>H, <sup>13</sup>C, and <sup>15</sup>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. Copyright © 2008 John Wiley & Sons, Ltd.

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## Introduction

The NMR is a powerful tool in determining the preferred conformation, the stereochemistry of a compound, and the stereoselectivity of reactions.<sup>[1]</sup> 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.<sup>[2]</sup> 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 <sup>1</sup>H NMR and UV spectroscopy.<sup>[3]</sup> 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 <sup>1</sup>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 <sup>1</sup>H and <sup>13</sup>C spectra of alkenes and imines was based on one- and two-dimensional NMR experiments. The connectivities were established by means of homonuclear

<sup>1</sup>H–<sup>1</sup>H (COSY) and heteronuclear <sup>1</sup>H–<sup>13</sup>C (HETCOR) correlation spectroscopy. The selected pulse sequence was applied because a high resolution in <sup>13</sup>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<sub>2</sub>, and CH<sub>3</sub> groups in compounds **1b–e**, **2b–e**, **3b–e**, and **4b–e**.

The exocyclic substituent (R<sub>2</sub>) 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  $20 \,^{\circ}C.^{[4]}$  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

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Scheme 1. Structure of olefins (1a-1e) and imines (2a-4e).



Scheme 2. Preferential orientation of the aryl group (a) in olefins and (b) in imines.



**Scheme 3.** Aliphatic region of the <sup>1</sup>H NMR spectrum of the imine compound **3d**. From top to bottom spectra with ytterbium tris[3-(triflouromethylhydroxymethylene)-(+)- camphorate]) in relation 1:9, simulated and experimental spectra with the corresponding assignments.

| Table 1. <sup>1</sup> H NMR chemical shifts of olefins (1) and ketimines (2, 3, and 4) |          |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--|----------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|  | HC=      | :    | 2    | :    | 3    |      | 4    | !    | 5    | (    | 6    | 7    | 8    | 9    | 10   | 11   | 12   | Me   |
|  |          | eq   | ах   |      |      |      |      |      |      |      |
| 1a   | 6.22     | 2.25 | 2.25 | 1.54 | 1.54 | 1.59 | 1.59 | 1.64 | 1.64 | 2.37 | 2.37 | -    | 7.19 | 7.29 | 7.16 | 7.29 | 7.19 | -    |
| 1bZ  | 6.18     | -    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | -    | 0    | 0    | 0    | 0    | 0    | 1.20 |
| 1bE  | 6.20     | -    | 2.26 | 1.83 | 1.25 | 1.76 | 1.41 | 1.68 | 1.51 | 2.73 | 1.96 | -    | 7.19 | 7.30 | 7.13 | 7.30 | 7.19 | 1.15 |
| 1d   | 6.23     | 2.33 | 2.22 | 1.83 | 1.12 | _    | 1.60 | 1.75 | 1.01 | 2.86 | 1.92 | -    | 7.19 | 7.29 | 7.17 | 7.29 | 7.19 | 0.92 |
| 1e   | 6.21     | 2.38 | 2.19 | 1.84 | 1.16 | -    | 1.22 | 1.92 | 1.05 | 2.96 | 1.84 | -    | 7.20 | 2.29 | 7.16 | 7.29 | 7.20 | 0.86 |
| 2a   | -        | 2.46 | 2.46 | 1.83 | 1.83 | 1.62 | 1.62 | 1.64 | 1.64 | 2.16 | 2.16 | -    | 8.07 | -    | 8.29 | 7.20 | 7.06 | -    |
| 2d   | -        | 2.56 | 2.45 | 2.02 | 1.40 | -    | 1.77 | 1.84 | 1.15 | 2.43 | 1.98 | -    | 8.06 | -    | 8.31 | 7.22 | 7.07 | 0.98 |
| 2e   | -        | 2.62 | 2.42 | 2.12 | 1.44 | _    | 1.40 | 1.95 | 1.18 | 2.50 | 1.92 | -    | 8.07 | -    | 8.31 | 7.23 | 7.08 | 0.89 |
| 3a   | -        | 2.45 | 2.45 | 1.84 | 1.84 | 1.61 | 1.61 | 1.65 | 1.65 | 2.16 | 2.16 | -    | 6.72 | 7.27 | 7.03 | 7.27 | 6.72 | -    |
| 3bZ  |          |      | 2.48 | 2.04 | 1.43 | 1.61 | 1.56 | 1.81 | 1.45 | 2.46 | 1.88 |      |      |      |      |      |      | 1.22 |
| 3d   | -        | 2.54 | 2.38 | 1.97 | 1.36 | _    | 1.71 | 1.78 | 1.10 | 2.45 | 1.88 | -    | 6.70 | 7.25 | 7.01 | 7.25 | 6.70 | 0.95 |
| 3e   | -        | 2.59 | 2.36 | 2.08 | 1.41 | _    | 1.36 | 1.89 | 1.14 | 2.54 | 1.83 | -    | 6.72 | 7.27 | 7.03 | 7.27 | 6.72 | 0.90 |
| 4a   | -        | 2.28 | 2.28 | 1.73 | 1.73 | 1.64 | 1.64 | 1.64 | 1.64 | 2.29 | 2.29 | 3.26 | 1.58 | 0.93 | -    | -    | -    | -    |
| 4d   | -        | 2.35 | 2.24 | 1.88 | 1.24 | _    | 1.73 | 1.87 | 1.10 | 2.77 | 1.83 | 3.19 | 1.58 | 0.93 | -    | -    | -    | 0.95 |
|  |          |      |      |      |      |      |      |      |      |      |      | 3.16 |      |      |      |      |      |      |
| 4e   | -        | 2.41 | 2.22 | 1.96 | 1.29 | -    | 1.34 | 1.97 | 1.15 | 2.86 | 1.75 | 3.27 | 1.63 | 0.93 | -    | -    | -    | 0.88 |
|  |          |      |      |      |      |      |      |      |      |      |      | 3.23 |      |      |      |      |      |      |
| o, ove   | rlapped. |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |

these isomers (E:Z) was 10:1 for the 2-methylcyclohexanone derivatives (**1b**, **2b**, **3b**, and **4b**). The signals of both isomers overlapped, which complicated the assignment of the minor isomer. The isomer relation for the 3-methylcyclohexanone derivatives was 10:9 (E:Z) (**1c**, **2c**, **3c**, and **4c**). The spectra showed overlapped resonances for both isomers, which made complete assignment difficult. The assignment of the atoms in the cyclohexenyl moiety was based on the *cis/trans*-to-lone-pair and the exocyclic substituent effects.

# Discussion

## <sup>1</sup>H NMR

In the present work, it was necessary to simulate the proton spectra<sup>[5]</sup> of the compounds (**1a**, **1d**, **1e**, **2a**, **2d**, **2e**, **3a**, **3d**, **3e**, **4a**, **4d** and **4e**) in order to correctly assign the compounds giving rise to the NMR data obtained. This was due to the complexity of the results, which arose from the similarity of the chemical shifts and the complicated coupling patterns – the signals of most of the protons reveal up to five different couplings to other protons. The assignment was performed considering the chemical shifts, the multiplicity, and the connectivity.

The data shown in Table 1 indicate that the proton chemical shifts of methylene C2 and C6 are similar for alkenes (**1a**, **1d**, and **1e**) and aliphatic imines (**4a**, **4d**, and **4e**), and that the inductive effect of nitrogen is similar to that corresponding to a phenyl group (C2 methylene). The same behavior is observed for the steric interaction and diamagnetic protection (C6 methylene). The  $\Delta\delta$  of protons bonded to C2 between alkenes (**1a**, **1d**, and **1e**) and imines derived from aromatic amines (**2a**, **2d**, **2e**, **3a**, **3d**, and **3e**) is 0.19  $\pm$  0.02 ppm (being greater for imines), whereas for protons bonded to C6, the  $\Delta\delta$  is about 0.43  $\pm$  0.03 ppm for *equatorial* protons (being greater for the corresponding alkenes). There are no significant differences between *axial* protons. The preceding data show that while in olefins the orientation of the phenyl group

is such that the diamagnetic current shifts the protons at high frequency, the corresponding orientation in the imine group shifts protons at a lesser frequency, which is only possible when the orientation of the phenyl group is on the same plane in olefins but perpendicular in imines (Scheme 2).

The coupling constant data listed in Table 2 for protons bonded to C4 ( ${}^{3}J_{H4ax,H3ax} = 12.1 \pm 0.7$ ;  ${}^{3}J_{H4ax,H3ec} = 3.0 \pm 0.5$ ;  ${}^{3}J_{H4ax,H5ec} = 2.8 \pm 0.8$ ; and  ${}^{3}J_{H4ax,H5ax} = 12.9 \pm 1.8$ ) make it possible to determine the chair conformation of the six-atom ring. The magnitude of the methyl group coupling constant of the **2b** isomer *Z* ( ${}^{3}J_{H,H} = 7.2$  Hz), as well as its  ${}^{13}$ C chemical shift, allows the determination of the axial preference.

The enantiomers *Ra* and *Sa* became nonequivalent as a result of the addition of ytterbium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate]) to compound **3d**. Consequently, the resonance of 5-methyl could be distinguished and the chemical shift effect observed was attributed to the fact that the chemical shift reagent coordinated only one of the two enantiomers. This result could be deduced because the methyl signal was enhanced upon increasing the concentration of the chemical shift reagent (Scheme 3).

## <sup>13</sup>C NMR

The complete assignments of the <sup>13</sup>C NMR spectra for all the isomers of the olefins (1a-e) and imines (2a-e, 3a-e, and 4a-e) are shown in Table 3. These assignments were made considering the effects of the substituents, the orientations, the connectivity, and the isomeric abundances for the 2- and 3-methylcyclohexanone derivatives (1b, 1c, 2b, 2c, 3b, 3c, 4b, and 4c).

Analysis of the substituent effects on the atoms of the aliphatic ring was performed considering the chemical shifts of the compounds derived from cyclohexanone (**1a**, **2a**, **3a**, and **4a**).

The inductive effect on the cyclohexenyl atoms is greater for imines than for alkenes, with the order being *N*-3-pyridyl

| Table 2.                     | 1H NMR coupling constants of selected olefins and imine derivatives |      |      |      |      |             |      |        |      |           |  |
|------------------------------|---|------|------|------|------|-------------|------|--------|------|-----------|--|
| <sup>2</sup> Ј <sub>НН</sub> | 1b <i>E</i>   | 1d   | 1e   | 2d   | 2e   | 3b <i>E</i> | 3d   | 3e     | 4d   | 4e        |  |
| 2.2                          |   | 12.2 | 12.2 | 12.4 | 12.4 |             | 12.4 | 12.4   | 12.4 | 14.0      |  |
| 2,2                          | - 12.4  | 13.2 | 13.3 | 13.4 | 13.4 | -           | 13.4 | 13.4   | 13.4 | 14.0      |  |
| 5,5<br>4 4                   | 13.4  | 15.1 | 12.4 | 12.0 | 12.4 | 12.1        | 12.0 | 15.1   | 15.1 | 15.0      |  |
| 4,4<br>5 5                   | 12.5  | -    | -    | 12.4 | -    | 11.8        | 12.0 | - 12.1 | 12.4 | -<br>12.4 |  |
| 5,5                          | 12.0  | 12.0 | 12.4 | 13.4 | 12.2 | 11.4        | 12.9 | 12.1   | 13.4 | 13.4      |  |
| 0,0                          | 13.7  | 15.4 | 15.5 | 13.7 | 13.9 | 12.7        | 13.7 | 13.4   | 11.4 | 14.0      |  |
| <sup>3</sup> Ј <sub>НН</sub> | _   | _    | _    | _    | _    | _           | _    | _      | 11.9 | 11.9      |  |
| H,CH₃                        | 6.5   | 6.5  | -    | 6.5  | _    | 6.7         | 6.6  | -      | 6.6  | -         |  |
| 2ax,3ax                      | 13.2  | 13.2 | 12.5 | 13.1 | 14.0 | 13.1        | 13.1 | 13.8   | 13.2 | 13.1      |  |
| 2ax,3eq                      | 4.4   | 4.4  | 4.6  | 5.5  | 5.2  | 4.3         | 5.3  | 5.2    | 5.2  | 5.5       |  |
| 2eq,3ax                      | -   | 3.6  | 3.9  | 3.2  | 3.7  | 0.5         | 4.0  | 3.7    | 4.4  | 4.2       |  |
| 2eq,3eq                      | -   | 3.4  | 3.1  | 4.5  | 3.1  | -           | 3.2  | 3.2    | 3.6  | 3.6       |  |
| 3ax,4ax                      | 11.4  | 11.4 | 12.0 | 11.4 | 12.4 | 12.8        | 11.1 | 12.1   | 11.2 | 12.8      |  |
| 3ax,4eq                      | 3.6   | -    | -    | -    | -    | 3.0         | -    | -      | -    | -         |  |
| 3eq,4ax                      | 4.8   | 3.1  | 2.3  | 3.0  | 2.5  | 3.5         | 3.0  | 2.5    | 3.1  | 2.6       |  |
| 3eq,4eq                      | 2.9   | -    | -    | _    | _    | 4.0         | -    | -      | -    | -         |  |
| 4ax,5ax                      | 11.8  | 11.1 | 13.5 | 11.1 | 14.1 | 11.1        | 11.1 | 14.7   | 11.8 | 12.5      |  |
| 4ax,5eq                      | 3.6   | 3.1  | 2.0  | 2.8  | 2.7  | 3.6         | 2.8  | 2.8    | 2.9  | 2.7       |  |
| 4eq,5ax                      | 4.7   | -    | -    | -    | -    | 3.5         | -    | -      | -    | -         |  |
| 4eq,5eq                      | 3.7   | -    | -    | -    | -    | 4.5         | -    | -      | -    | -         |  |
| 5ах,бах                      | 11.9  | 13.2 | 13.1 | 13.2 | 13.6 | 11.1        | 13.2 | 13.5   | 13.2 | 13.7      |  |
| 5ax,6eq                      | 4.9   | 3.3  | 4.2  | 4.0  | 3.7  | 4.7         | 4.0  | 4.2    | 3.8  | 3.4       |  |
| 5eq,6ax                      | 4.4   | 4.8  | 4.0  | 4.7  | 5.1  | 3.1         | 4.7  | 5.2    | 5.1  | 5.2       |  |
| 5eq,6eq                      | 4.1   | 4.1  | 2.0  | 3.0  | 2.6  | 3.0         | 3.0  | 2.6    | 3.1  | 3.4       |  |
| 7,8                          | -   | -    | -    | -    | -    | -           | -    | -      | 7.5  | 7.5       |  |
| 8,9                          | 7.4   | 7.3  | 7.3  | -    | -    | 7.3         | 7.9  | 7.9    | 7.5  | 7.5       |  |
| 9,10                         | 7.6   | 7.4  | 7.4  | -    | -    | 7.3         | 7.4  | 7.3    | -    | -         |  |
| 10,11                        | -   | -    | -    | 4.8  | 4.8  | -           | -    | -      | -    | -         |  |
| 11,12                        | -   | -    | -    | 8.0  | 8.0  | -           | -    | -      | -    | -         |  |
| <sup>4</sup> Ј <sub>НН</sub> |   |      |      |      |      |             |      |        |      |           |  |
| HC=,2ax                      | 1.3   | 2.0  | 1.8  | _    | -    | -           | -    | -      | -    | -         |  |
| HC=,2eq                      | -   | 0.5  | n.d. | _    | -    | -           | -    | -      | -    | -         |  |
| HC <del>=</del> ,6ах         | 1.8   | 1.8  | 2.0  | -    | -    | -           | -    | -      | -    | -         |  |
| HC <del>=</del> ,6eq         | 1.4   | 1.5  | n.d. | -    | -    | -           | -    | -      | -    | -         |  |
| 2eq,6eq                      | -   | 2.4  | 2.2  | 2.3  | 2.3  | -           | 2.3  | 2.4    | 2.2  | 2.4       |  |
| 2eq,6ax                      | 0.5   | 0.5  | 0.5  | n.d. | 0.3  | 0.5         | 0.3  | 0.3    | 0.6  | 0.7       |  |
| 3eq,5eq                      | 0.6   | 2.3  | 2.4  | 2.9  | 3.0  | 2.0         | 2.9  | 3.0    | 2.9  | 3.0       |  |
| 3eq,5ax                      | n.d.  | n.d. | n.d. | 0.5  | n.d. | n.d.        | 0.5  | n.d.   | -    | n.d.      |  |
| 4eq,6eq                      | 0.9   | n.d. | -    | n.d. | -    | 0.8         | n.d. | -      | n.d. | -         |  |
| 4еq,бах                      | 0.5   | n.d. | -    | n.d. | -    | n.d.        | n.d. | -      | n.d. | -         |  |
| 4ах,бах                      | n.d.  | 0.5  | n.d. | n.d. | n.d. | n.d.        | n.d. | n.d.   | n.d. | 0.7       |  |
| 7,9                          | -   | -    | -    | _    | -    | -           | _    | -      | 0.5  | 0.5       |  |
| 8,10                         | 1.3   | 1.2  | 1.3  | 0.2  | 0.2  | 1.3         | 1.3  | 1.3    | -    | -         |  |
| 8,12                         | -   | -    | -    | 2.6  | 2.6  | -           | -    | -      | -    | -         |  |
| 10,12                        | -   | -    | -    | 1.6  | 1.5  | -           | -    | -      | -    | -         |  |
| °Ј <sub>НН</sub>             |   |      |      |      |      |             |      |        |      |           |  |
| HC=,9                        | 1.0   | 1.0  | n.d. | -    | -    | -           | -    | -      | -    | -         |  |
| HC=,11                       | 1.0   | 1.0  | -    | -    | -    | -           | -    | -      | -    | -         |  |
| 8,11                         | _   | -    | -    | 0.8  |      | -           | -    | -      | -    | -         |  |
| n.d., Not observed.          |   |      |      |      |      |             |      |        |      |           |  |

> *N*-phenyl > *N*-propyl > C-phenyl. The *syn/anti* effect of the substituent bonded to the exocyclic atom generates a  $\Delta\delta$  value between C2 and C6 of about 8.2 ± 0.1 ppm. The stronger steric effect of the propyl group in compounds **4a** to **4e** shifts C6 to a lower frequency compared to other compounds.

The low-frequency chemical shifts of C4 ( $\delta = 20 \pm 1$  ppm) and C2 ( $\delta = 34.5 \pm 1$  ppm) in the 2-methylcyclohexanone derivatives (**1b**, **2b**, **3b**, and **4b**) of the *Z* isomer are a result of the  $\gamma_{\text{axial}}-\gamma_{\text{gauche}}$  ( $\Delta \delta = 4.5 \pm 1.0$  ppm) effect of the methyl substituent. The  $\gamma_{\text{equatorial}}$  effect on C6 of the *E* isomer of the

| Table | e 3. | <sup>13</sup> C NMR chemical shifts of olefins and imine derivatives |        |       |       |       |       |       |        |        |        |        |        |        |
|-------|------|--|--------|-------|-------|-------|-------|-------|--------|--------|--------|--------|--------|--------|
|       |      | HC=  | 1      | 2     | 3     | 4     | 5     | 6     | 7      | 8      | 9      | 10     | 11     | Me     |
| 1a    | a    | 122.14   | 143.63 | 37.87 | 28.83 | 26.89 | 28.08 | 29.65 | 138.60 | 129.12 | 128.19 | 125.97 | _      |        |
| 1b    | Ζ    | 147.48   | 121.98 | 33.64 | 29.05 | 21.03 | 33.24 | 30.80 | 139.04 | 128.85 | 128.25 | 126.01 | -      | 18.66  |
|       | Ε    | 147.73   | 119.66 | 39.19 | 37.03 | 25.64 | 28.55 | 29.22 | 139.04 | 129.23 | 128.18 | 125.91 | -      | 19.04  |
| 1c    | Ζ    | 122.31   | 143.05 | 37.32 | 27.70 | 35.32 | 34.15 | 37.85 | 138.59 | 129.12 | 128.20 | 125.97 | -      | 22.67  |
|       | Ε    | 122.39   | 143.10 | 46.17 | 34.77 | 35.20 | 27.00 | 29.06 | 138.66 | 129.12 | 128.20 | 125.97 | -      | 22.51  |
| 10    | k    | 122.25   | 143.23 | 37.21 | 36.93 | 32.86 | 36.20 | 28.91 | 139.18 | 129.13 | 128.20 | 125.98 | -      | 22.27  |
| 1e    | 9    | 121.83   | 143.55 | 37.79 | 29.43 | 48.43 | 28.74 | 29.48 | 138.60 | 129.13 | 128.20 | 125.97 | -      | 32.79  |
|       |      |  |        |       |       |       |       |       |        |        |        |        |        | 27.84  |
| 2a    | a    | -  | 174.91 | 39.28 | 27.75 | 25.66 | 27.54 | 31.15 | 150.64 | 119.74 | 128.68 | 122.87 | -      |        |
| 2b    | Ζ    | -  | 178.74 | 34.91 | 27.89 | 20.05 | 33.43 | 33.48 | 150.31 | 119.11 | 128.74 | 122.70 | -      | 17.47  |
|       | Е    | -  | 176.69 | 41.48 | 36.27 | 24.77 | 27.99 | 30.62 | 151.19 | 119.37 | 128.50 | 122.40 | -      | 16.84  |
| 2c    | Ζ    | -  | 174.90 | 39.12 | 26.55 | 34.44 | 34.54 | 39.42 | 151.11 | 120.25 | 129.16 | 123.08 | -      | 22.41  |
|       | Е    | -  | 175.13 | 47.79 | 34.97 | 34.44 | 26.64 | 30.93 | 151.23 | 120.25 | 129.20 | 123.24 | -      | 22.53  |
| 20    | k    | -  | 175.38 | 38.93 | 36.17 | 32.31 | 35.94 | 30.73 | 151.28 | 120.27 | 129.21 | 123.40 | -      | 21.83  |
| 26    | 9    | -  | 175.63 | 39.40 | 28.88 | 47.82 | 28.74 | 31.17 | 151.23 | 120.36 | 129.20 | 123.42 | -      | 28.05  |
|       |      |  |        |       |       |       |       |       |        |        |        |        |        | 32.86  |
| 3a    | a    | -  | 176.78 | 39.05 | 27.48 | 25.13 | 27.27 | 31.03 | 146.20 | 141.12 | 144.07 | 123.11 | 127.09 |        |
| 3b    | Ζ    | -  | 181.40 | 35.44 | 28.40 | 20.28 | 33.85 | 34.13 | 146.53 | 141.07 | 144.50 | 123.65 | 126.56 | 17.34  |
|       | Е    | -  | 178.93 | 42.08 | 36.65 | 25.05 | 28.42 | 31.31 | 147.3  | 141.39 | 144.34 | 123.52 | 127.14 | 17.04  |
| 3с    | Ζ    | -  | 176.99 | 39.14 | 26.00 | 33.72 | 34.16 | 38.66 | 146.39 | 141.36 | 144.36 | 123.45 | 127.19 | 21.80  |
|       | Е    | -  | 177.18 | 47.29 | 34.50 | 33.72 | 26.17 | 31.09 | 146.49 | 141.31 | 144.36 | 123.45 | 127.24 | 21.90  |
| 30    | ł    | -  | 177.05 | 38.26 | 35.40 | 31.45 | 35.17 | 30.21 | 146.34 | 141.23 | 144.23 | 123.22 | 126.95 | 20.97  |
| 36    | 9    | -  | 178.00 | 39.35 | 28.78 | 47.58 | 28.65 | 31.30 | 146.87 | 141.88 | 144.82 | 123.81 | 127.68 | 32.75  |
|       |      |  |        |       |       |       |       |       |        |        |        |        |        | 27.92  |
| 4a    | a    | -  | 171.39 | 39.42 | 27.29 | 25.64 | 26.51 | 28.09 | 51.40  | 23.72  | 11.40  | -      | -      |        |
| 4b    | Z    | -  | 176.49 | 35.52 | n.d.  | 20.38 | 32.83 | 30.95 | 51.41  | 24.40  | 12.12  | -      | -      | 16.903 |
|       | E    | -  | 175.10 | 42.01 | 35.95 | 24.44 | 27.53 | 27.43 | 52.00  | 24.31  | 12.03  | -      | -      | 17.417 |
| 4c    | Z    | -  | 171.89 | 39.14 | 25.98 | 34.14 | 33.28 | 36.44 | 51.82  | 24.01  | 11.77  | -      | -      | 21.83  |
|       | E    | -  | 172.00 | 47.93 | 34.20 | 34.16 | 25.48 | 27.69 | 51.91  | 24.01  | 11.77  | -      | -      | 21.98  |
| 40    | ł    | -  | 172.21 | 39.08 | 35.84 | 32.25 | 35.04 | 27.64 | 52.15  | 24.25  | 12.02  | -      | -      | 21.52  |
| 46    | 9    | -  | 173.16 | 39.83 | 28.59 | 48.01 | 27.93 | 28.53 | 52.51  | 24.60  | 12.39  | -      |        | 32.78  |
|       |      |  |        |       |       |       |       |       |        |        |        |        |        | 27.91  |
|       |      |  |        |       |       |       |       |       |        |        |        |        |        |        |

n.d., not determined.

| Table 4. <sup>15</sup> N NMR of imine derivatives <sup>a</sup>   |                                     |                                   |                                     |                        |                            |  |  |  |  |  |
|--|-------------------------------------|-----------------------------------|-------------------------------------|------------------------|----------------------------|--|--|--|--|--|
| Comp.  | δ ( <sup>3</sup> J <sub>N,H</sub> ) | Comp.                             | δ ( <sup>3</sup> J <sub>N,H</sub> ) | Comp.                  | $\delta ({}^3J_{\rm N,H})$ |  |  |  |  |  |
| 2a   | -73.32 (7.78)                       | 3a                                | -74.34 (7.7)                        | 4a                     | -64.66 (7.03)              |  |  |  |  |  |
| <b>2b</b> ( <i>E</i> )   | -73.35                              | 3b                                | n.d.                                | <b>4b</b> ( <i>E</i> ) | -64.78 (5.4)               |  |  |  |  |  |
| <b>2c</b> ( <i>E</i> , <i>Z</i> )  | -71.62, -71.90                      | <b>3c</b> ( <i>E</i> , <i>Z</i> ) | -73.71, -73.94                      | <b>4c</b> (E or Z)     | -64.33                     |  |  |  |  |  |
| 2d   | -73.03 (4.84)                       | 3d                                | -73.90 (7.4)                        | 4d                     | -63.81 (5.3)               |  |  |  |  |  |
| 2e   | -73.7 (7.5)                         | 3e                                | n.d.                                | 4e                     | -65.17                     |  |  |  |  |  |
| <sup>a</sup> The <sup>15</sup> N– <sup>1</sup> H three-bond coupling constant is via N=C–C–H, with the hydrogen <i>syn</i> to lone pair. |                                     |                                   |                                     |                        |                            |  |  |  |  |  |

"The "N = C - C - H, with the hydrogen syn to n.d., not determined.

preceding compounds is about  $-0.55 \pm 0.10$  ppm, whereas the  $\gamma_{\text{equatorial}}$  effect of the methyl group on C5 of the *E* isomer (**1b**, **2b**, **3b**, and **4b**) is  $0.70 \pm 0.30$  ppm. The equivalent effect on the 3-methylcyclohexanone derivatives (**1c**, **2c**, **3c**, and **4c**) is about  $-0.40 \pm 0.15$  ppm for both isomers.

4-methylcyclohexanone derivatives (**1d, 2d, 3d**, and **4d**), the equivalent effect is about  $-0.55 \pm 0.20$  ppm.

## <sup>15</sup>N NMR

The  $\gamma_{\text{equatorial}}$  effect on C3 (*Z* isomer) or C5 (*E* isomer) of the methyl group of the 3-methylcyclohexanone derivatives (**1c, 2c, 3c**, and **4c**) is  $-1.20 \pm 0.20 \text{ ppm}$ , whereas for the

The <sup>15</sup>N chemical shift (Table 4) showed a slight variation for compounds **1a** to **2d.** Signals of both geometric isomers of the imine (E/Z) were observed in compounds **1c** and **2c**. The chemical

shift effect of the nitrogen atom of the pyridine group in C2 can be neglected; however, in the compound containing the propylimine group, a shift of about 8.5  $\pm$  0.5 ppm is observed.

Observation of the  ${}^{15}N-{}^{1}H$  coupling constants for some of the compounds was only possible by means of INEPT nondecoupling pulse sequence. Splitting was greater than 4.8 Hz and was found to be in agreement with the lone pair *syn* effect.<sup>[6]</sup>

## Conclusions

Aryl groups have a preferential rotamer that is co-planar to the carbon–carbon double bonds, whereas in imine compounds, the aryl group predominates at a position that is orthogonal to the carbon–nitrogen double bond. Cyclohexane exchanges rapidly in compounds that do not contain a substituent, but in compounds with a substituent it prefers the conformation with an alkyl group at C3 or C4 (at the *equatorial* position). However, when the methyl group is at C2, it prefers the *axial* position. To the best of our knowledge, this is the first article that shows a chiral axis in exocyclic ketimines.

## **Experimental Section**

NMR spectra of compounds **1a** to **4e** were recorded at ±18 °C using a Bruker 300 Avance spectrometer equipped with a 5-mm multinuclear probe. All spectra were obtained using a CDCl<sub>3</sub> solution (0.9 mmol of the compound per 0.4 ml of solvent). The chemical shifts were referenced<sup>[7]</sup> to internal (CH<sub>3</sub>)<sub>4</sub>Si ( $\delta$  <sup>1</sup>H = 0,  $\delta$  <sup>13</sup>C = 0) and neat CH<sub>3</sub>NO<sub>2</sub> ( $\delta$  <sup>15</sup>N for  $\Xi$  <sup>15</sup>N = 10.136767 MHz). <sup>1</sup>H NMR spectra were recorded at 300 MHz (spectral width: 6188.1 Hz, acquisition time: 2.648 s, 16 384 data points, equivalent 30° pulse duration, 16 scans, recycle delay: 1 s). <sup>13</sup>C{<sup>1</sup>H} NMR spectra were recorded at 75.47 MHz (spectral width: 17 361.1 Hz, 32 768 data points, equivalent to 30° pulse duration, 256 scans, recycle delay: 0.01 s). Similar conditions were used for the APT and INEPT spectra.

<sup>15</sup>N NMR spectra of compounds **2a** to **4e** were recorded at 30.38 MHz by using INEPT methods<sup>[8]</sup> (spectral width: 15 151.6 Hz; 16 384 data points, from 1024 to 13 706 scans, depending on the solubility; recycle delay: 4 s, the delays were optimized in agreement with  ${}^{3}J_{\text{NH}}$ ).

 $^1H-^1H$  COSY spectra were obtained with the cosy45 pulse sequence<sup>[9]</sup> using a 1024  $\times$  512 data point matrix and a 751.20  $\times$  751.20 Hz frequency matrix. The recycle delay was 2 s and a total of 16 scans were performed. Fourier transformations were carried out for F1 and F2 using a sine function in the absolute-value mode.

 $^{13}C^{-1}H$  COSY spectra were obtained with the HETCOR pulse sequence for the aliphatic region<sup>[9]</sup> using a 2048 × 256 data point matrix and a 6265 × 751 Hz frequency matrix. The pulse time intervals 1 and 2 were set as 2 × 1/4J = 1.85 ms. The recycle delay was 2 s and a total of 16 scans were performed. Fourier transformations were carried out using a square-sine function for F1 and F2 in the absolute-value mode.

MS studies of compounds **2a** to **4e** were carried out using a Hewlett-Packard 5890 spectrometer coupled to a gas chromatograph in the El mode (at 70 eV). No mass spectra could be obtained for compounds **1a** to **1e** because of their instability at their respective boiling temperatures.

#### <sup>1</sup>H NMR assignments

The chemical shifts and spin-spin coupling constants of the protons of the cyclohexane rings were determined by means of computer simulations<sup>[5]</sup> carried out considering subsystems of ten nuclei. In the case of the methyl groups, the number of spins was reduced by symmetry because the three hydrogen atoms are chemically and magnetically equivalent. The root-mean-square (r.m.s.) error between the experimental and simulated spectra was 0.11 Hz. Excellent correlation was observed with the experimental spectrum when the long-range coupling constants ( ${}^{4}J_{H,H}$  and  ${}^{5}J_{H,H}$ ) were taken into account.

#### **Synthesis**

Schiff bases were prepared by condensation of equimolar amounts of the corresponding amines and cyclohexanones in methylene chloride (**4a** to **4e**) or toluene (**2a** to **3e**) solutions. The reaction was carried out under reflux (for 12 h) in a Dean-Stark water separator. The compounds were purified by means of low-pressure distillation.

Alkenes (**1a** to **1e**) were prepared through the Wittig reaction from benzyl triphenyl phosphonium and the corresponding cyclohexanone in a dry dimethyl sulfoxide (DMSO) solution, using NaH as base. The compounds were purified by using a chromatography silica gel column and hexane as eluting agent.

The physical and spectroscopic properties of **1a**,<sup>[10]</sup> **2a**,<sup>[11]</sup> and **2b**<sup>[12]</sup> are in good agreement with previous reports. These properties are listed in the Supplementary Material.

#### **Supporting information**

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

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