SYNTHESIS OF NEW *N*-PHENYL-*N*-(1-PHENYLHEX-5-EN-1-YL)ACETAMIDES AND THEIR ^{1}H-NMR CONFORMATIONAL STUDY

SÍNTESE DE NOVAS N-FENIL-N-(1-FENILHEX-5-EN-1-IL)ACETAMIDAS E O SEU ESTUDO CONFORMACIONAL POR ^{1}H-RMN

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Abstract

The synthesis and characterization of different *N*-phenyl-*N*-(1-phenylhex-5-en-1-yl)acetamides is presented. Two conformational isomers were observed for one of the compounds in their ^{1}H/^{13}C-NMR spectra. Computational calculations and dihedral angle comparison using the allylic system coupling constants (*J*) were carried out to determine the isomeric structures responsible for signals duplicity and chemical shifting.

Key words: acetamides, conformational isomers, computational calculation, NMR, Garbisch equation.

Resumo

A síntese e caracterização de diferentes *N*-fenil-*N*-(1-fenilhex-5-en-1-il) acetamidas é presentada. Dois isómeros comformacionaisforam observados para um dos compostos no seu espectro de $^{1}H/^{13}C$-RMN. Cálculos computacionais e comparação de ángulos diedros usando as constandes de acoplamento (*J*) para o sistema alílicoforam realizadas para determinar as estructuras isoméricasresponsáveis pela duplicidade de sinais e o deslocamento químico.

Palavras-chave: acetamidas, isómeros conformacionais, cálculo computacional, RMN, equação de Garbisch.

Introduction

Target oriented synthesis (TOS) is one of the most important methodologies in organic chemistryto access biologically active compounds (1). Molecules including quinoline and tetrahidroquinoline derivatives are widely known for their biological and pharmacological activity as well as for their uses in organic electronics (2). Previous reports from our research group have shown both antifungal and antiparasitic activities of *N*-phenyl-α-2-propen-1-yl benzenpropanamines**1a-e** (3-4). The use of **1a** as synthon for different *N*-heterocycles containing the tetrahydrolepidine and quinolinemoiety is well known. These substances are similar to isolated compounds from *Galipealongiflora* and *Galipeaofficinalis*, which have been studied and used against fever, dysentery, malaria and leishmaniasis treatment, among others (5-12).

Literature reports have shown that acetylation of *N*-(prop)butenylamines turns these compounds into biologically active *N*-(prop)butenylacetamides (3,13-14). Thus, new *N*-phenyl-*N*-(1-phenylhex-5-en-1-yl)acetamides**2a-f** were prepared by *N*-acetylation of compounds **1a-f**. Their synthesis and $^{1}H/^{13}C$-NMR data is discussed and presented. Biological activity of compounds **2a-f** is currently under study.

Experimental section (Materials and methods)

IR spectra were obtained on a FT-IR Bruker Tensor 27, using KBr windows. IR main signals are condensed in **Table 1**. GC/MS data were acquired on a HP5890A Series II gas chromatography equipped with a HP-5MS column (5% methyl phenyl siloxane, 30m x 0.25mm x 0.25µm) and a selective mass detector HP5972 (EI, 70 eV). NMR spectra were recorded on aBruker Avance-400. Coupling constants *J* are reported in Hertz. See **Scheme 1** for ^{1}H, ^{13}C assignment.

*General procedure for the synthesis of N-phenyl-N-(1-phenylhex-5-en-1yl) acetamides**2a-f***

A round bottom flask with a reflux condenser, a thermometer and a magnetic stirrer was filled with 0.35 g (1.24 mmol) of *N*-phenyl-α-2-propen-1-ylbenzenpropanamine (previously prepared) (3) and 3.80 g (37.02 mmol) of acetic anhydride. The reaction mixture was refluxed for 4-6 h and neutralized using $NaHCO_3$. NaOH 0.1 M was used to adjust the mixture to pH 12. Ethyl acetate was used for extraction (20 mL x 3). The organic layer was dried over Na_2SO_4, the solvent removed and the crude product purified by column

chromatography on SiO_2 using *n*-heptane and ethyl acetate gradient mixtures. Compounds characterization was carried out using IR, ^{1}H, ^{13}C NMR and GC-MS.

N-phenyl-*N*-(1-phenylhex-5-en-1-yl)acetamide**2a**

From *N*-phenyl-α-2-propen-1-ylbenzen propanamine**1a** (0.33 g, 1.31 mmol) and acetic anhydride (4.32 g, 42.30 mmol). Pure compound **2a** was obtained after column chromatography as a brownish oil. R_f= 0.50 (*n*-heptane:AcOEt, 5:2). MS [EI, 70 eV] (*m/z*, %): 293 ($M^{+\cdot}$,2), 252 (38), 210 (100), 117 (13), 91 (47). δ_H ppm ($CDCl_3$, 400 MHz): 1.62 (td, ^{3}J= 8.0, 7.3, $2H_5$), 1.72 (s, $3H_{4c}$), 2.03-2.19 (m, $\underline{2H_3}$), 2.63 (ddd, ^{2}J= 14.4; ^{3}J= 8.3, 7.6, $1H_6$), 2.71 (ddd, ^{2}J=14.4; ^{3}J= 8.3, 7.6, $1H_6$), 4.90-5.05 (m, $3H_{1,4}$), 5.76 (dddd, ^{3}J= 17.7, 9.5, 6.8, 6.4, $1H_2$), 6.94-7.39 (m, $10H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $23.63_{(4c)}$, $33.13_{(6)}$, $34.57_{(5)}$, $37.75_{(3)}$, $54.07_{(4)}$, $117.11_{(1)}$, $125.86_{(p)}$, $128.25_{(2xm)}$, $128.36_{(2xo)}$, $128.74_{(p')}$, $129.36_{(2xm')}$, $129.86_{(2xo')}$, $135.66_{(2)}$, $139.37_{(i')}$, $141.81_{(i)}$, $171.03_{(4b)}$.

N-Phenyl-*N*-(4-methylphenylhex-5-en-1-yl)acetamide**2b**

From of *N*-(4-methylphenyl)-α-2-propen-1-ylbenzenpropanamine **1b** (1.07 g, 4.03 mmol) and acetic anhydride (10.79 g, 105.75 mmol). Pure compound was obtained after chromatography column as a brownish oil. R_f= 0.50 (*n*-heptane:AcOEt, 5:2). MS [EI, 70 eV] (*m/z*, %): 307 ($M^{+\cdot}$,2), 266 (37), 224 (100), 150 (11), 91 (40). δ_H ppm ($CDCl_3$, 400 MHz): 1.68 (td, ^{3}J= 8.1, 7.3, $2H_5$), 1.79 (s, $3H_{4c}$), 2.08-2.29 (m, $\underline{2H_3}$), 2.39 (s, $3H_{4d}$), 2.70

(ddd, ^{2}J= 14.5; ^{3}J= 8.1, 7.5, $1H_6$), 2.77 (ddd, ^{2}J= 14.5; ^{3}J= 8.1, 7.5, $1H_6$), 4.93-5.18 (m, $3H_{1,4}$), 5.83 (dddd, ^{3}J= 17.5, 9.3, 6.9, 6.5, $1H_2$), 7.06 (d, ^{3}J= 8.2, $2H_{o'}$), 7.14-7.33 (m, $7H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $20.98_{(4d)}$, $23.47_{(4c)}$, $33.04_{(6)}$, $34.46_{(5)}$, $37.69_{(3)}$, $53.80_{(4)}$, $116.95_{(1)}$, $125.75_{(p)}$, $128.17_{(2xm)}$, $128.27_{(2xo)}$, $129.51_{(2xo')}$, $129.90_{(2xm')}$, $135.64_{(2)}$, $136.49_{(p')}$, $138.18_{(i')}$, $141.79_{(i)}$, $171.16_{(4b)}$.

N-Phenyl-*N*-(4-methoxyphenylhex-5-en-1-yl)acetamide**2c**

From *N*-(4-methoxyphenyl)-α-2-propen-1-ylbenzenpropanamine **1c** (0.35 g, 1.24 mmol) and acetic anhydride (3.67 g, 35.96 mmol). Pure product was obtained after chromatography column as a brownish oil. R_f= 0.40 (*n*-heptane:AcOEt, 5:2). MS [EI, 70 eV] (*m/z*, %): 323 ($M^{+\cdot}$, 2), 282 (28), 240 (100), 91 (51). δ_H ppm ($CDCl_3$, 400 MHz): 1.67 (td, ^{3}J= 8.1, 7.3, $2H_5$), 1.80 (s, $3H_{4c}$), 2.06-2.30 (m, $\underline{2H_3}$), 2.70 (ddd, ^{2}J= 14.4; ^{3}J= 8.3, 7.6, $1H_6$), 2.77 (ddd, ^{2}J=14.4; ^{3}J= 8.3, 7.6, $1H_6$), 3.83 (s, $3H_{4d}$), 4.98-5.14 (m, $3H_{1,4}$), 5.83 (dddd, ^{3}J=17.6, 9.5, 6.8, 6.5, $1H_2$), 6.92 (d, ^{3}J= 9.2, $2H_{o'}$), 7.04-7.35 (m, $7H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $23.55_{(4c)}$, $33.12_{(6)}$, $34.54_{(5)}$, $37.72_{(3)}$, $53.78_{(4)}$, $55.43_{(4d)}$, $114.43_{(2xm')}$, $117.06_{(1)}$, $125.87_{(p)}$, $128.27_{(2xm)}$, $128.39_{(2xo)}$, $130.87_{(2xo')}$, $131.75_{(i')}$, $135.76_{(2)}$, $141.88_{(i)}$, $159.20_{(p')}$, $171.57_{(4b)}$.

N-Phenyl-*N*-(4-bromophenylhex-5-en-1-yl) acetamide**2d**

From *N*-(4-bromophenyl)-α-2-propen-1-ylbenzenpropanamine **1d** (0.68 g, 2.06 mmol) and acetic anhydride (7.34 g, 71.91 mmol). Pure product was obtained after column chromatography as a brownish oil. R_f= 0.47 (*n*-heptane:AcOEt, 5:2). MS [EI, 70 eV] (*m/z*, %): 373 ($M^{+\cdot}$,2), 330 (33), 290 (95), 288 (100), 91 (82). δ_H ppm ($CDCl_3$, 400 MHz): 1.61-1.73 (m, $2H_5$), 1.79 (s, $3H_{4c}$), 2.17 (ta, ^3J= 7.0, $\underline{2H_3}$), 2.65-2.79 (m, $2H_6$),4.94-5.13 (m, $3H_{4,1}$), 5.81 (dddd, ^3J=17.2, 10.1, 6.6, 6.3, $1H_2$), 7.06 (d, ^3J= 8.8, $2H_{o'}$), 7.14-7.31 (m, $5H_{Arom}$), 7.55 (d, ^3J= 8.8, $2H_{m'}$). δ_C ppm ($CDCl_3$, 100 MHz): $23.63_{(4c)}$, $33.07_{(6)}$, $34.59_{(5)}$, $37.55_{(3)}$, $54.07_{(4)}$, $117.31_{(1)}$, $122.39_{(p')}$, $125.95_{(p)}$, $128.21_{(2xm)}$, $128.41_{(2xo)}$, $131.55_{(2xo')}$, $132.62_{(2xm')}$, $135.44_{(2)}$, $138.42_{(i')}$, $141.53_{(i)}$, $170.67_{(4b)}$.

N-Phenyl-*N*-(4-fluorophenylhex-5-en-1-yl)acetamide**2e**

From *N*-(4-fluorophenyl)-α-2-propen-1-ylbenzenpropanamine **1e** (0.63 g, 2.34 mmol) and acetic anhydride (6.80 g, 66.62 mmol). Pure product was obtained after column chromatography as a brownish oil. R_f= 0.43 (*n*-heptane:AcOEt, 5:2). MS [EI, 70 eV] (*m/z*, %): 311 ($M^{+\cdot}$,2), 270 (36), 228 (100), 117 (15), 91 (51). δ_H ppm ($CDCl_3$, 400 MHz): 1.71-1.82 (m, $2H_5$), 1.87 (s, $3H_{4c}$), 2.22-2.28 (m, $\underline{2H_3}$), 2.79 (ddd, ^2J= 13.8; ^3J= 9.6, 6.9, $1H_6$), 2.84 (ddd, ^2J= 13.8; ^3J= 9.6, 6.9, $1H_6$), 5.06-5.22 (m, $3H_{1,4}$), 5.91 (dddd, ^3J= 17.0, 10.6, 6.6, 6.3, $1H_2$), 7.16-7.40 (m, $9H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $23.55_{(4c)}$, $33.03_{(6)}$, $34.53_{(5)}$, $37.52_{(3)}$, $53.89_{(4)}$, $116.28_{(2xm')}$ (d, ^2J= 22.5), $117.21_{(1)}$, $125.91_{(p)}$, $128.18_{(2xm)}$, $128.38_{(2xo)}$, $131.55_{(2xo')}$, $135.19_{(i')}$ (d, ^4J= 3.4), $135.49_{(2)}$, $141.57_{(i)}$ $162.07_{(p')}$ (d, ^1J=249.1), $171.02_{(4b)}$.

N-Phenyl-*N*-(2-methylphenylhex-5-en-1-yl)acetamide**2f**

From *N*-(2-methylphenyl)-α-2-propen-1-ylbenzen propanamine**1f** (0.67 g, 2.52 mmol) and acetic anhydride (7.23 g, 70.81 mmol). Pure product was obtained after column chromatography as a brownish oil. R_f= 0.53 (*n*-heptane:AcOEt, 5:2). GC showed a single signal. MS [EI, 70 eV] (*m/z*, %): 307 ($M^{+\cdot}$, 2), 266 (39), 224 (100), 118 (13), 91 (51). NMR data for **α conformer**: δ_H ppm ($CDCl_3$, 400 MHz): 1.73 (s, $3H_{4c}$), 1.74-1.82 (m, $2H_5$), 2.26 (s, $3H_{4d}$), 2.45-2.51; 2.52-2.59 (m, $\underline{2H_3}$), 2.59-2.67 (m, $2H_6$), 4.75-4.86 (m, $1H_4$), 5.08-5.20 (m, $2H_1$), 5.89 (dddd, ^3J= 17.3, 9.9, 6.7, 6.5, $1H_2$), 7.07-7.34 (m, $9H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $18.44_{(4d)}$, $23.15_{(4c)}$, $33.45_{(6)}$, $33.57_{(5)}$, $38.23_{(3)}$, $55.87_{(4)}$, $117.08_{(1)}$, $125.81_{(p)}$, $126.87_{(m')}$, $128.21_{(p')}$, $128.25_{(2xo)}$, $128.32_{(2xm)}$, $129.64_{(o')}$, $131.54_{(m'')}$, $135.93_{(2)}$, $136.87_{(i')}$, $139.35_{(o'')}$, $141.67_{(i)}$, $171.06_{(4b)}$. NMR data for **β conformer**: δ_H ppm ($CDCl_3$, 400 MHz): 1.49-1.61 (m, $2H_5$), 1.77 (s, $3H_{4c}$), 1.86-2.07; 2.36-2.48 (m, $\underline{2H_3}$), 2.27 (s, $3H_{4d}$), 2.77 (ta, ^3J= 8.4, $2H_6$), 4.75-4.86 (m, $1H_4$), 4.95-5.01 (m, $2H_1$), 5.69 (dddd, ^3J= 16.6, 10.8, 7.9, 6.0, $1H_2$), 7.07-7.34 (m, $9H_{Arom}$). δ_C ppm ($CDCl_3$, 100 MHz): $18.49_{(4d)}$, $23.06_{(4c)}$, $33.14_{(6)}$, $33.31_{(5)}$, $36.61_{(3)}$, $55.83_{(4)}$, $117.18_{(1)}$, $125.81_{(p)}$, $126.95_{(m')}$, $128.17_{(p')}$, $128.24_{(2xo)}$, $128.34_{(2xm)}$, $129.32_{(o')}$, $131.60_{(m'')}$, $135.42_{(2)}$, $137.02_{(i')}$, $139.22_{(o'')}$, $141.97_{(i)}$, $171.04_{(4b)}$.

Conformational analysis

Ten chemically reasonable structures for compound **2f** were used as the starting point for energy minimization using the Parameterized Model 3 (PM3) semiempirical method (15). Geometry optimization and vibrational frequency calculations (for verifying that the

structures correspond to minima on the potential energy surface) were then carried out using the B3LYP functional with the 6-31+G(2d,p) basis set as implemented in Gaussian 09 (16-24). Seven different possible conformer structures $\mathbf{2f_1}$-$\mathbf{2f_7}$ were found. Energy differences [kcal/mol] for all minima were calculated with and without vibrational zero point energies (VZPE).

Results and discussion

Scheme1 shows the synthesis of new 1-phenylhex-5-en-1-ylacetamides **2a-f** from *N*-butenylamines**1a-f** using acetic anhydride as both reagent and solvent, under reflux (140 ºC). Acetamides**2a-f** were easily obtained with yields between 66-92%. Optimal reaction time was established by both TLC and GC in about 4-6 h. Main IR vibration bands of allyl C=C-H and acetamide C=O are listed in **Table 1**. IR N-H tension and flexion bands in compounds **1a-f** clearly disappeared after acetyl protection.

Scheme 1. Synthesis of acetamides**2a-f** (see labels for ^{1}H and ^{13}C-NMR assignments in experimental section).

Table 1. IR [*v*, cm^{-1}] main signals for compounds **2a-f**.

	***v*(C=O)**	***v*(C=CH)**	***v*(=C-H) Aromatic *p*-disubstituted**	***v*(=C-H) Aromatic monosubstituted**
2a	1655	915	----	745-701
2b	1655	915	824	749-700
2c	1653	916	837	750-700
2d	1658	917	833	749-700
2e	1658	917	844	750-700
2f	1658	917	763*	749-700

* *o*- disubstitued

GC-MS (EI, 70eV) data are condensed in **Table 2**. Molecular ions corresponding to molecular mass of **2a-f** appeared in all cases with low intensity; base peak Φ_2 results after consecutive allyl [Φ_1] and acetyl [$(\Phi_1\text{-}C_2H_3O]^+$ fragmentation. Benzyl fragment Φ_3 (*m/z* 91) is characteristic in all compounds.

Table 2. MS (EI, 70eV) [m/z (int. %)] main fragments for compounds **2a-f**.

	$\mathbf{M^{\cdot+}}$	$\mathbf{\Phi_1}$ **,** $\mathbf{[M\text{-}C_3H_5]^+}$	$\mathbf{\Phi_2}$ **,** $\mathbf{[\Phi_1\text{-}C_2H_3O]^+}$	$\mathbf{\Phi_3}$**,** $\mathbf{[C_7H_7]^+}$
2a	293 (2)	252 (38)	210 (100)	91 (47)
2b	307 (2)	266 (37)	224 (100)	91 (40)
2c	323 (2)	282 (28)	240 (100)	91 (51)
2d	373 (2)	330 (33)	288(100)	91 (82)
2e	311 (2)	270 (33)	228 (100)	91 (51)
2f	307 (2)	266 (39)	224 (100)	91 (51)

^1H, ^{13}C and 2D NMR experiments confirmed the structures of compounds **2a-f**. Due to a short relaxation time in ^{13}C- APT NMR spectra for *Co'*, a broad signal appeared; thus, in **2e**

it was not possible to assign the correct *C o'-F* coupling constant. Diastereotopic protons H_{3a} and H_{3b} appeared in ^{1}H-NMR as a multiplet from 1.86 ppm to 2.59 ppm in all cases. Correct assignment of allyl-H_2 coupling constants and multiplicity for compounds **2a-f** was completed by comparative simulation considering a first order spectra ($\Delta\nu/J > 8$) of an AA'MXX' spin system (25); spin simulation was carried out using Mestrenova v7.1.1 (test version) (26). Determined experimental values of chemical shifts and coupling constants range for the allyl system were used to simulate the H_2 signal until an identical multipletwas obtained by direct comparison, as shown in **Figure 1**.

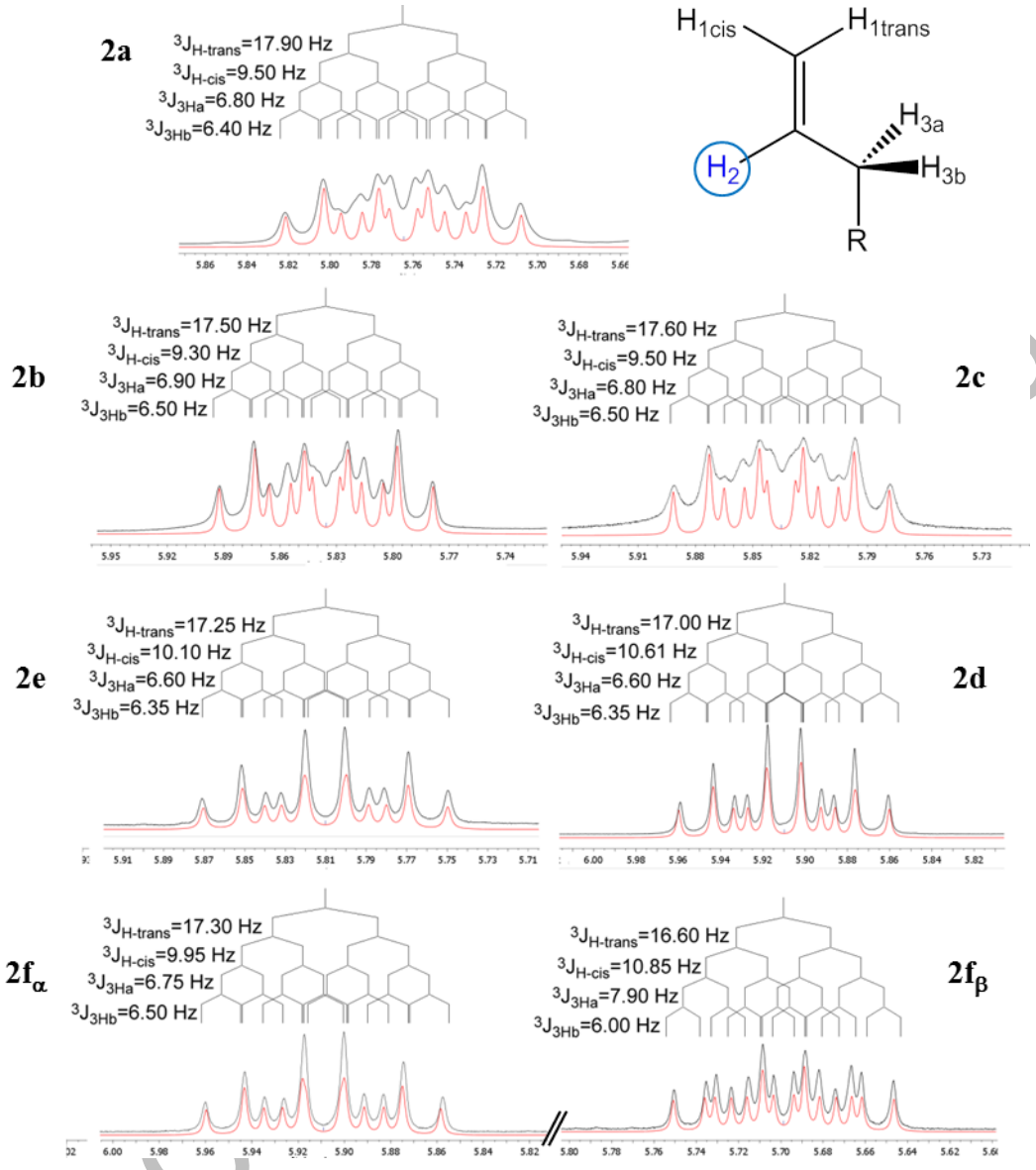


Figure 1. Obtained (black) and simulated (red) spectra for allyl-*H_2* proton considering an AA'MXX' spin system.

H_2 proton chemical shifts and coupling constants for **2a-f** allyl system are shown in **Table 3**. Compound **2f** showed a single GC signal but a double group of signals in ^{1}H and ^{13}C-NMR; characteristic coupling constants for the allyl H_2 proton were observed due to the existence of two different conformational isomers (α/β).

Table 3. ^{1}H-NMR chemical shifts [ppm] and coupling constants ^{3}J [Hz] for the allyl H_2nuclei of **2a-f**.

Compound	δ [ppm]	^{3}J (H_{trans})	^{3}J (H_{cis})	$^{3}J(H_{3a})$	$^{3}J(H_{3b})$
2a	5.765	17.90	9.50	6.80	6.40
2b	5.834	17.50	9.30	6.90	6.50
2c	5.834	17.60	9.50	6.80	6.50
2d	5.811	17.25	10.10	6.60	6.35
2e	5.907	17.00	10.61	6.60	6.35
2fα	5.898	17.30	9.95	6.75	6.50
2fβ	5.696	16.60	10.85	7.90	6.00

^{1}H-NMR integral relation of conformers **2f$_{\alpha}$**and **2f$_{\beta}$** was 1:1.15 (**Figure 2**). ^{1}H-NMR experiments showed that α and β conformational isomers ratio does not change in time at room temperature. Conformers **2f$_{\alpha}$**and **2f$_{\beta}$**also showed diastereotopic protons H_{3a} and H_{3b} as separated multiplets.

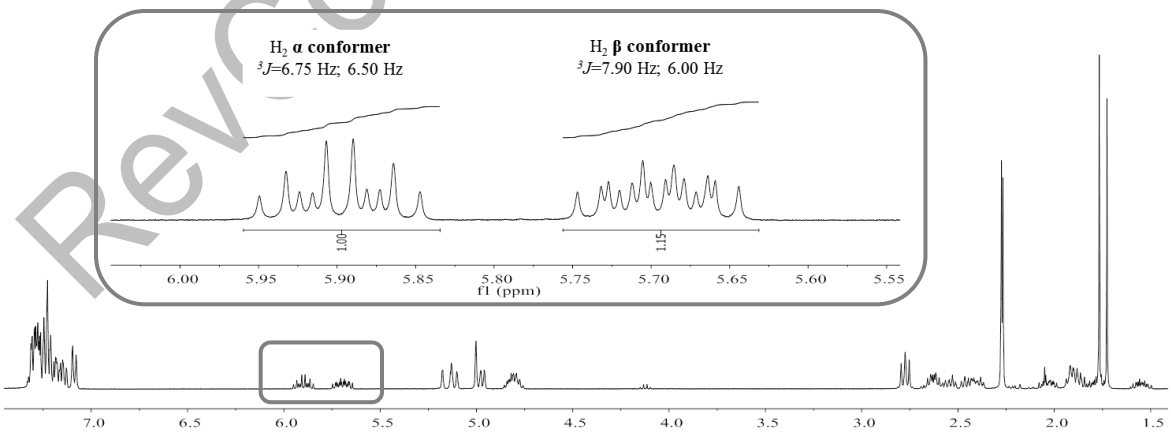


Figure 2.^{1}H-NMR ($CDCl_3$, 400MHz) spectra of **2f**; the two different allyl- H_2 signals (in expansion) determine the α/β conformers.

After conformational analysis of **2f**, despite of including both, the electronic energy and the VZPE differences, the optimized structures **$2f_1$-$2f_7$** showed similar ΔE values, avoiding a direct assignment to explain the duplicity of the signals in ^{1}H-NMR. Molden was used for displaying the molecular structures (27). These structures are qualitatively similar, differing mainly on the allyl group dihedral angles and slightly on rotation of other sigma bonds (**Figure 3**).

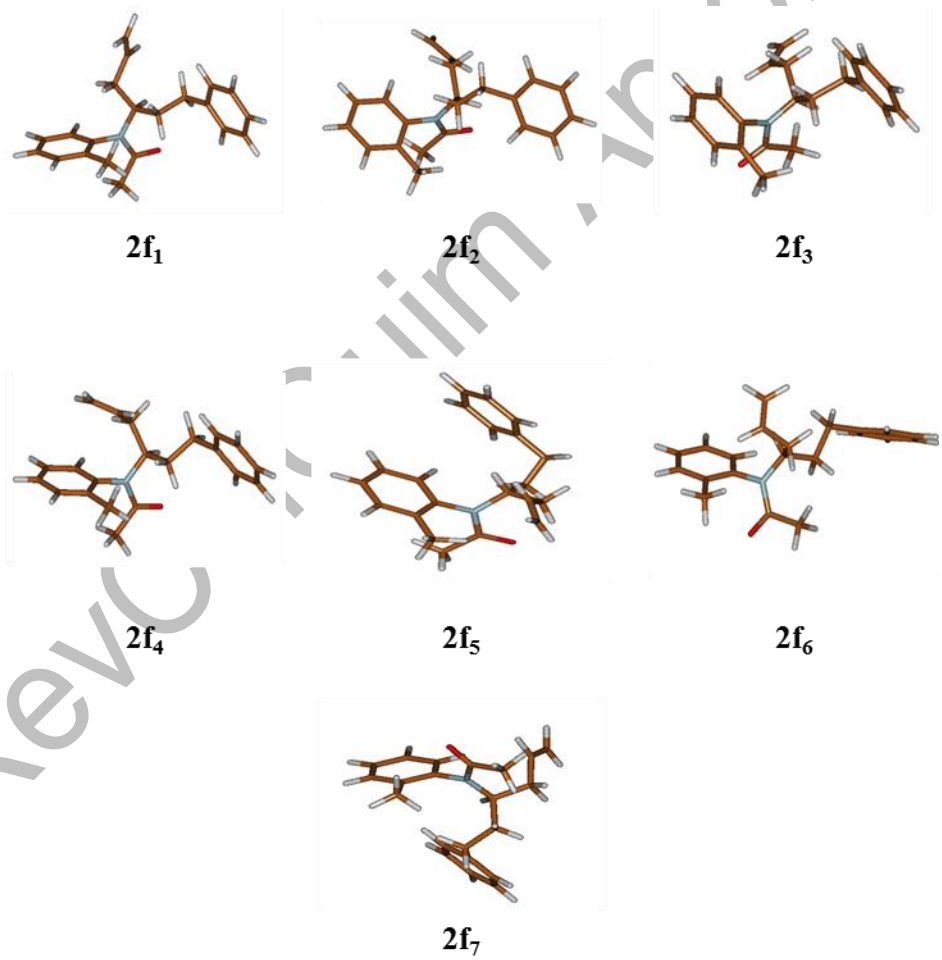


Figure 3. Calculated structures for conformers **$2f_{1-7}$**

Table 4 shows the energies and the allyl group dihedral angles for each **2f** conformer after optimization, taking **$2f_2$** [lowest electronic energy at the B3LYP(6-31+G(2d,p)) level of theory] as reference for energetic differences.

Table 4. Calculated energy values and allyl group dihedral angles (degrees) for seven different conformers of **2f**.

	ΔE [Kcal/mol] (electronic energy)	**Total ΔE [Kcal/mol] (including VZPE)**	**Dihedral angles [degrees °]**	
			Φ_1	**Φ_2**
$2f_1$	0.47	**0.46**	63	179
$2f_2$	0	**0**	170	286
$2f_3$	1.79	**2.02**	64	179
$2f_4$	2.05	**2.16**	66	181
$2f_5$	1.08	**1.11**	173	295
$2f_6$	5.08	**5.25**	66	182
$2f_7$	4.85	**5.46**	62	178

To correlate the H_2 allyl ^{1}H-NMR signals to a particular conformer, the proposed equation by Garbisch for allyl compounds [**Eq. 1]** was used (28). Garbisch equation is a modified Karplus equation involving also σ and π bonds contributions. Some authors suggest that some modifications can be done to make this equation more precise (29-31). With the Garbish equation a relation between observed coupling constants (*J*) and the dihedral angle (Φ) for the allylic proton H_2 and H_3 for each conformer was determined, as shown in **Tables 5** and **6**.

Table 5.Coupling constants ^{3}J [Hz] and their corresponding dihedral angles (Φ_1 and Φ_2) from Garbisch equation for allyl protons H_2 and H_{3a}/H_{3b} in compounds **2a-e**.

Compound	$^{3}J_{H3a}$	$^{3}J_{H3b}$	Φ_1 [±15º]	Φ_2 [±15º]
2a	6.4	6.8	12.9	133
2b	6.5	6.9	9.1	134
2c	6.5	6.8	9.1	133
2d	6.3	6.6	0.4	130
2e	6.3	6.6	0.4	130

Dihedral angles for conformers $\mathbf{2f_{1\text{-}7}}$ found in our calculations and conformers $\mathbf{2f_{\alpha}}$ and $\mathbf{2f_{\beta}}$ obtained from Garbisch equation are not equivalent, but approximated (**Table 6**) considering ±15° of uncertainty (27).

Table 6. Dihedral angles ($\mathbf{\Phi_1}$ y $\mathbf{\Phi_2}$) for allyl protons H_2 and H_{3a}/H_{3b} in seven different conformers for **2f**; calculated using the B3LYP(6-31+G(2d,p)) level of theory (left) and from the Garbisch equation (right).

$$^{3}J \cong \begin{cases} 6.6cos^2\Phi + 2.6sen^2\Phi (0º \leq \Phi \leq 90º) \\ 11.6cos^2\Phi + 2.6sen^2\Phi (180º \geq \Phi \geq 90º) \end{cases} \text{[Eq. 1]}$$

	Calculated results							Garbisch's results	
	$\mathbf{2f_1}$	$\mathbf{2f_3}$	$\mathbf{2f_4}$	$\mathbf{2f_6}$	$\mathbf{2f_7}$	$\mathbf{2f_2}$	$\mathbf{2f_5}$	**α**	**β**
$\mathbf{\Phi_1}$	63	64	66	66	62	170	173	9.1	140
$\mathbf{\Phi_2}$	179	179	181	182	178	286	295	133	232

A comparison for both models (**Figure 4**) shows high similarity when a Newman representation of the allylH_2 and vicinal methylenic protons H_{3a} and H_{3b} are depicted. Considering this fact, it was possible to associate these two different positions for H_{3a} and

H_{3b} protons to conformers α and β according to the observed ^{1}H and ^{13}C-NMR spectra, concluding that bulky groups (R and C=C) are located in a pseudo bisecting conformation in Newman's projections (**Figure 4**).

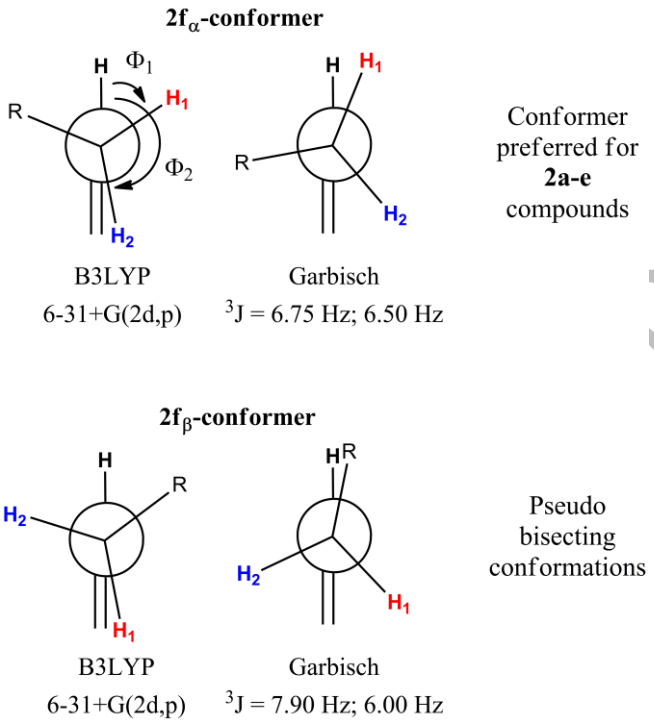
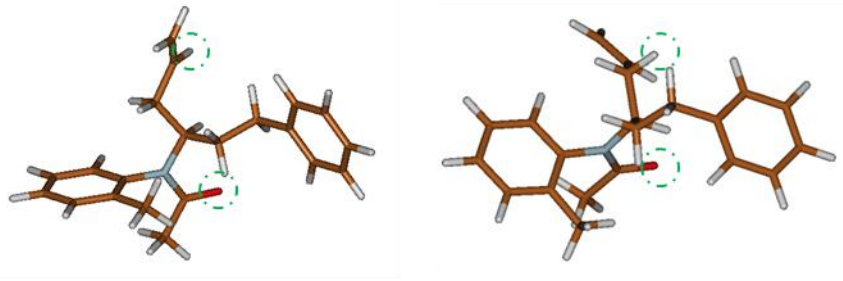


Figure 4. Newman projections for allyl group conformers **2f$_\alpha$** and **2f$_\beta$**: left, calculated structures (B3LYP/6-31+G(2d,p); right, according to [**Eq. 1**].

Thus, possible structures of α/β conformers were established according to their calculated energy, in each case. Allyl group disposition according to Garbisch equation was within the approximation limits with calculated conformers **2f$_1$** and **2f$_2$** (**Figure 5**).



Conformer **2f$_\alpha$** (2f$_1$) Conformer **2f$_\beta$** (2f$_2$)

Figure 5. Calculated structures (B3LYP/6-31+G(2d,p) for conformers α and β of **2f**.

Analogous calculated structures for **2f** differ basically on the spatial distribution of the allyl group and its dihedral angle; a 2.72 Å dipolar interaction between the allyl proton and the acetyl oxygen atom was observed in conformer **2f$_\beta$** (**Figure 6**), explaining the chemical shifting to high fields in the ^{1}H-NMR spectrum due to C=O anisotropic protection. Each conformer of **2f (**α and β) was totally elucidated using 2D-NMR experiments (COSY, HSQC and HMBC).

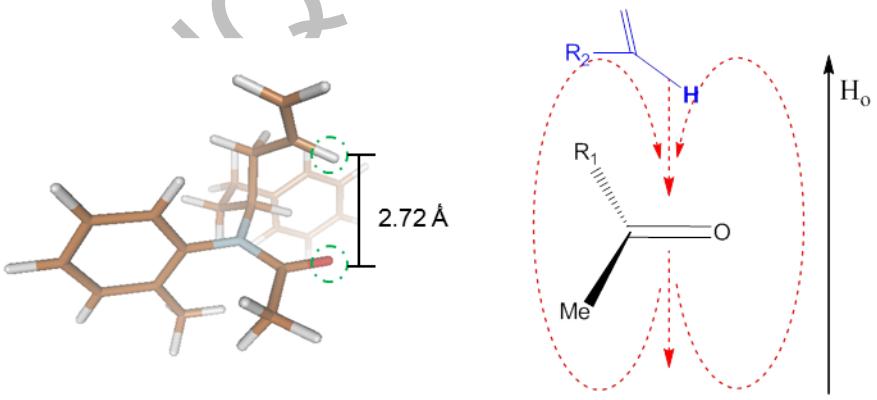


Figure 6. Left: Allyl-*H$_2$* proton interaction at 2.72 Å distance with the carbonyl oxygen in conformer **2f$_\beta$**. Right: the diamagnetic protection zone of double bond C=O.

Conclusions

An easy methodology to access new *N*-phenyl-*N*-(1-phenylhex-5-en-1-yl) acetamides**2a-f** using acetic anhydride as reagent and solvent, including green chemistry principles was used. Using quantum chemical calculations and Garbisch's approximation it was possible to determine that compounds **2a-e** prefer a single conformation similar to conformer **2f$_\alpha$**. Existence of conformers **2f$_\alpha$** and **2f$_\beta$** explain the double signals observed in both ^{1}H and ^{13}C-NMR spectra for compound **2f**. Coupling constants and chemical shifts values for H_2 allyl proton signals of compounds **2a-f** were described for each conformer and can be used as a comparative base in ^{1}H-NMR allyl-H_2 signal coupling constants assignation.

Acknowledgments

Authors express their acknowledgment to Universidad Industrial de Santander-UIS DIEF (internal project 5171) for financial support.

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